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**ESTABLISHMENT OF A CENTER FOR ENVIRONMENTAL MEDICINE  
AT THE MEDICAL COLLEGE OF OHIO, TOLEDO, OHIO**

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## TABLE OF CONTENTS

	<u>Page No.</u>
Summary .....	2
Molecular Toxicology Division .....	3
Carcinogenicity and Tumor Promoting Activity of Trichloroethylene in B6C3F1 Mice .....	4
Dose-Response Relationship for Trichloroethylene: 56 Day Study of Trichloroethylene .....	6
Respiratory Toxicology Division .....	7
Program 1. Dispersion of Aerosol and Gaseous Toxins Throughout the Tracheobronchial Tree .....	8
Program 2A. Gene Expression Related to the Metabolism of Toxins . . .	9
Program 2B. Bronchial Inflammatory Mediators of the Inhalation Injuries .....	11
Program 2C. Pulmonary Microvascular Vasoreactivity in Relation to Systemic Absorption of Inhaled Toxins .....	12
Architectural Program for the Building to House the Center for Environmental Medicine .....	13
Appendix 1. Biographical Sketches for Key Personnel of the Center for Environmental Medicine	
Appendix 2. Program Document for the Building for the Center for Environmental Medicine	

## SUMMARY

The Center for Environmental Medicine has been established at the Medical College of Ohio, Toledo, Ohio with Dr. Michael A. Pereira, Ph.D. as Director. The Center consists of two divisions, i.e. Molecular Toxicology and Respiratory Toxicology. The Molecular Toxicology Division has initiated studies to better understand the carcinogenic activity of compounds of interest to the U.S. Air Force. These studies have emphasized trichloroethylene, a major contaminant around Air Force bases. A letter of agreement with Wright-Patterson Air Force Base is being formalized so as to allow their collaboration. Studies that have been initiated include 1) demonstration of the tumor promoting activity of trichloroethylene in mouse liver; 2) determination of the molecular mechanism for the tumor promoting activity of trichloroethylene; and 3) determination of the biochemical molecular activity of trichloroethylene in mouse liver. The Respiratory Toxicology Division has initiated the following studies: Program information has been obtained to determine the appropriate site, space needs, design criteria and project cost for a building to house the Center for Environmental Medicine.

The Center for Environmental Medicine at the Medical College of Ohio was established by the Board of Trustees on March 25, 1991. Dr. Michael A. Pereira was recruited to be Director of the Center for Environmental Medicine as well as Director of the Division of Molecular Toxicology. Dr. Dan E. Olson joined the Center for Environmental Medicine as Director of Respiratory Toxicology. Ms. Marilyn Cline was appointed Administrative Assistant/Secretary for the Center. The following personnel have joined the Center and their biographical sketches can be found in Appendix 1.

### **Molecular Toxicology Division**

Michael A. Pereira, Ph.D.	MCO
William T. Gunning, III, Ph.D.	MCO
James A. Hampton, Ph.D.	MCO
Yian Wang, M.D., Ph.D.	MCO

### **Respiratory Toxicology Division**

James C. Willey, M.D.	MCO
Dan E. Olson, M.D., Ph.D.	MCO
Gourie Shanker, Ph.D.	MCO, University of Toledo
Raj Sawhney, Ph.D.	MCO
Ken W. Cairns, M.S.	MCO
Erin Coy, M.S.	MCO
Patricia Metting, Ph.D.	MCO
Beverly Giammara, M.S.	MCO

Although the Center for Environmental Medicine is divided into two divisions, collaborative research is encouraged between them.

## **MOLECULAR TOXICOLOGY DIVISION**

In order to ensure that the work performed by the Center for Environmental Medicine under this grant with the U.S. Air Force is pertinent to the mission of the Air Force, Dr. Pereira met with the scientists at Wright-Patterson Air Force Base, Toxic Hazards Division, Armstrong Aerospace Medical Research Laboratory.. At this meeting, Dr. Pereira presented to Wright-Patterson Air Force Base the studies being proposed especially as related to trichloroethylene. One of the studies presented involved the evaluation of the toxicological and molecular activity of trichloroethylene in the liver of B6C3F1 mice from exposures up to 90 days. Wright-Patterson Air Force Base was proposing to perform a very similar study with trichloroethylene so that it was decided at this meeting to merge the two studies into one with Wright-Patterson Air Force Base performing the exposure to the mice. Tissues will be harvested at Wright-Patterson Air Force Base and evaluated for the effect of trichloroethylene upon cell proliferation and associated molecular events. Tissues will also be sent from Wright-Patterson Air Force Base to the Medical College of Ohio for evaluation of the effect of trichloroethylene upon apoptosis in the liver. A letter of agreement to allow this exchange of tissues between the two institutions was initiated at this time and is under formal review.

Wright-Patterson Air Force Base is presently establishing in their laboratory some of the molecular assays to be performed on the livers obtained from this study of trichloroethylene. These assays include immunohistochemical detection of growth factors and proto-oncogenes and in situ hybridization for determination of their expression. These assays are presently being established at Wright-Patterson Air Force Base. Dr. Pereira had some archived tissue from animals exposed to the metabolites of trichloroethylene, dichloroacetic acid and trichloroacetic acid. He has sent these tissues to Wright-Patterson Air Force Base for them to use as controls in the validation of the immunohistochemical procedures in their laboratory.

### **Carcinogenicity and Tumor Promoting Activity of Trichloroethylene in B6C3F1 Mice**

Trichloroethylene is an organic solvent used widely by industry and the U.S. Air Force as a metal degreaser and cold cleaner of fabricated metal parts. Although production has decreased over the last 25 years, it is still approximately 120 million pounds per year in the United States. This widespread use of trichloroethylene has resulted in multimedia environmental pollution with measurable quantities found in and near surface water, ground water, and soil as well as in high percentage of superfund sites. Contamination at and around bases has resulted in the U.S. Air Force spending millions of dollars a year in the control and clean-up of trichloroethylene.

In mice, trichloroethylene has been demonstrated to induce both liver and lung tumors and in rats, males had an excess of kidney tumors. This has resulted in the U.S. EPA proposing to classify trichloroethylene as a category B2 (probable human carcinogen). However, the Science Advisory Board of the U.S. EPA has stated that the evidence for the carcinogenicity of trichloroethylene falls rather on a continuum between category B2 and category C (possible human carcinogen). Recently, the American Conference of Governmental and Industrial Hygienists (ACGIH) has established the classification of trichloroethylene as a group A5 substance, not suspected as a human carcinogen. The ACGIH classification of trichloroethylene relied heavily upon the major epidemiological study performed on the cohort of over 14,000 workers at the Hill Air Force Base in Utah. The wide range in the classification of the carcinogenic hazard of trichloroethylene to humans is mainly due to differing opinions as to the applicability of the carcinogenic activity observed in mouse liver and in male rat kidney to estimate the potential carcinogenic hazard to humans. Under this grant, we have initiated a study to determine the mechanism and dose response relationship of the carcinogenic activity of trichloroethylene in mouse liver. The mechanistic studies will attempt to determine the extent to which the carcinogenic activity demonstrated in mouse liver is applicable to predicting the carcinogenic activity in humans and the dose response relationship studies will supply quantitative data to improve any risk assessment of trichloroethylene.

Female B6C3F1 mice were administered on day 15 of age either MNU (25 mg/kg bw) or DMBA (20  $\mu$ moles/kg bw). At 7 weeks of age, some of the mice started to receive trichloroethylene by corn oil gavage 5 days a week or DCA, TCA or a mixture of DCA and TCA in their drinking water. At 270 days of age, livers will be harvested from 20 of the animals in the high dose trichloroethylene, DCA and TCA groups. Also, the remaining 40 animals in these groups will stop receiving trichloroethylene, DCA or TCA. These three groups in which treatment will be terminated, are designed to demonstrate the reversal of precancerous lesions i.e., promoter dependent lesions, and to determine whether removal of the test agent results in a wave of apoptosis in these lesions. Animals in these groups will be

sacrificed at 2, 7, 14 and 94 days after the termination of treatment. It is proposed that inhibition by the test agents of apoptosis in precancerous lesions will cause a build up of cells primed to enter apoptosis. Upon termination of treatment, these cells will be released from this inhibition and proceed to undergo apoptosis. It is expected that the termination of trichloroethylene, DCA and TCA exposure will induce a wave of apoptosis at 2 days similar to rats. The wave of apoptosis will demonstrate that trichloroethylene and its metabolites inhibited apoptosis in precancerous lesions which could be the mechanism for promoter dependent lesions and would give these lesions an advantage to survive and expand in population.

The major sacrifice for this study will occur at 364 days of age. At necropsy, the liver will be examined for tumors of 5 mm or greater. These tumors will be harvested and a mid-section of the tumor obtained for histopathological evaluation. The rest of the tumor will be frozen in liquid nitrogen and stored at -75°C until analyzed. The median lobe will then be rapidly harvested, cut into blocks, placed in a mold, covered with O.C.T. (optimum cutting temperature compound), frozen on dry ice and stored at -75°C until used to obtain cryostatic sections. The remaining lobes of the liver will be harvested, fixed in formalin for no more than 24 hours, stored in 70% alcohol for up to 48 hours, and embedded in paraffin.

Precancerous lesions (foci of altered hepatocytes and hepatocellular adenomas) compared to non-involved hepatocytes, will be characterized using histopathological, immunohistochemical, biochemical and molecular criteria. The frozen specimens will be used for the determination of activated *ras* family oncogene and other biochemical and molecular markers of precancerous and cancerous lesions, that can not be evaluated using formalin fixed tissue. These markers include glucose-6-phosphatase, UDP-glucuronosyl-transferase, microsomal epoxide hydrolase, NADPH-cytochrome P450 reductase, CP2B1/2, CP2E1 and CP4A (Cytochrome P450 isoforms induced as a pleiotropic response to liver tumor promoters). To measure the extent of metabolism of trichloroethylene, precancerous lesions and non-involved areas can be dissected out of the frozen tissue blocks and along with the frozen tumors, used as a source for microsomes and cytosol. The formalin fixed tissue will be evaluated for precancerous lesions (foci of altered hepatocytes and hepatocellular carcinomas) and for hepatocellular carcinomas. This characterization will include apoptosis, cell proliferation, toxicity including lipid peroxidation, glycogen content and immunohistochemical determination of the modulation in the levels of glutathione s-transferase- $\pi$ , *c-fos*, *c-jun*, *c-myc*, TGF- $\alpha$ , and TGF- $\beta$ 1. An attempt will be made to describe the sequential occurrence in the modulation of the markers and endpoints in foci of altered hepatocytes, hepatocellular adenomas and then, hepatocellular carcinomas.

Some animals that were initiated with MNU or DMBA but not subsequently treated with any of the three test agents, as well as animals that were not initiated with either carcinogen but received the high dose of TCA, will be sacrificed at 537 days of age. The longer duration is required to obtain tumors large enough (>5.0 mm) to observe and harvest at necropsy. These tumors will be analyzed for the mutation spectrum in the activated *ras* oncogene family in order to determine the mutation spectrum for tumors induced in mouse liver by MNU, DMBA and TCA. Tumors obtained from animals that were initiated with MNU or DMBA and then promoted with one of the three test agents, will be evaluated to determine whether they contain the mutation spectrum distinctive of the initiating chemical. This would demonstrate whether trichloroethylene and its two metabolites promoted the occurrence of tumors derived from cells in which MNU/DMBA induced mutations in the *ras* oncogene family.

The tumors harvested at 537 days of age from TCA-treated animals, will be analyzed to determine the mutation spectrum in the *ras* oncogene family. The mutation spectrum will be compared to that found by us in tumors induced by DCA, trichloroethylene and tetrachloroethylene (Anna, *et al.*, 1994). Tumors induced by tetrachloroethylene (13%) but not trichloroethylene (1%), had an excess incidence of mutations in the *K-ras* oncogene. The activation of *K-ras* gene in the tumors induced by tetrachloroethylene could have been caused by oxidative damage to the DNA resulting from induced proliferation of peroxisomes by its metabolite, TCA. This comparison will attempt to indicate the extent to which TCA could be responsible for the hepatocarcinogenesis of these two chloroethylenes.

At conclusion of this study, we will have determined 1) the tumor-promoting activity of trichloroethylene; 2) the tumor-promoting activity of a mixture of two of trichloroethylene major metabolites, DCA and TCA, as a model for the carcinogenic activity resulting from the metabolism of trichloroethylene; 3) the differential sensitivity of precancerous lesions and non-involved hepatocytes to trichloroethylene and its metabolites with respect to enhancement of cell proliferation, proto-oncogene activation, and modulation of redox potential, metabolism and lipid peroxidation. The demonstration of a differential sensitivity of precancerous lesions compared to non-involved hepatocytes, would strongly support the proposed mechanism that trichloroethylene is carcinogenic in mouse liver by selectively expanding the size of the population of precancerous hepatocytes, and 4) the inhibition by trichloroethylene and its metabolites of apoptosis in precancerous lesions as demonstrated by a wave of apoptosis upon cessation of treatment with the test agents. The wave of apoptosis should occur in the precancerous lesions two days after the termination of treatment with trichloroethylene. In rats, the termination of treatment with other tumor promoters, resulted in the maximum increase in apoptosis at two days. Since these lesions compared to non-involved hepatocytes, also have an increased level of cell proliferation, the inhibition of apoptosis will further result in the selective expansion of the population of cells in these lesions, i.e. tumor promotion.

The same molecular and immunohistochemical markers will be evaluated in the 56 day dose-response study described next. Therefore, we will be able to determine 1) how well modulation of these markers predict carcinogenic activity and 2) whether the modulation of the marker by trichloroethylene occurs similarly after subchronic exposure as after chronic exposure in precancerous lesions and non-involved hepatocytes. It should be noted that this study will be continued under Air Force Grant No. F49620-94-1-0265 and is being performed in collaboration with the Air Force scientist at Wright-Patterson AFB.

#### **Dose-Response Relationship for Trichloroethylene: 56 Day study of trichloroethylene.**

At Wright-Patterson, AFB Major Stephen Channel has started the following study in collaboration with the Center for Environmental Medicine. Male B6C3F1 mice are being administered five days a weeks and by gavage either 0, 0 +corn oil, 400, 800 or 1200 mg/kg bw trichloroethylene. Animals are being sacrificed after 2, 3, 6, 10, 14, 21, 28, 35, 42, 49 and 56 days of treatment and the livers harvested and evaluated for cell proliferation (PCNA and mRNA histone-*in situ*), peroxisome proliferation, free radicals, lipid peroxidation, 8-hydroxyguanine levels, redox state, levels of ornithine decarboxylase and protein kinase C, and immunohistochemical quantitation of *c-fos*, *c-jun*, *c-myc*, TGF- $\alpha$ , and TGF- $\beta$ 1. At the Medical College of Ohio, we will determine the level of apoptosis, glycogen



content and synthesis, CYP2B1/2, CYP2E, CYP4A, glutathione S-transferase- $\pi$ , and the expression of mRNA for *c-fos*, *c-jun* and *c-myc*. This study will provide the U.S. Air Force with the dose-response and temporal relationships of trichloroethylene with respect to three of the proposed mechanisms for the carcinogenic activity in mouse liver, i.e. enhanced cell proliferation, inhibition of apoptosis and formation of a mutagenic adduct in DNA (8-hydroxyguanine) resulting from oxidative damage. The results of this experiment will be compared to the initiation-promotion study in order 1) to determine the relative sensitivity of acutely exposed hepatocytes, chronically exposed non-involved hepatocytes and precancerous hepatocytes (in lesions) to modulation of molecular markers by trichloroethylene; 2) to determine the ability of the molecular markers to predict the tumor promoting activity of trichloroethylene; and 3) to obtain an indication of the tumor promoting activity of dose levels of trichloroethylene lower than those suitable for use in the initiation-promotion study.

This study will be completed under Air Force Grant No. F49620-94-1-0265. Under this second Air Force Grant another study is being initiated to determine the effect of trichloroethylene upon earlier molecular events in mouse liver.

## RESPIRATORY TOXICOLOGY DIVISION

The Respirable Toxicology Division has initiated this investigation to better understand the *in vivo* concentration dependency of bronchial epithelial cell toxicity to inhaled gases and particulates. The project's goals relate to both basic science investigations into the fundamental mechanisms of inhaled toxin dispersion throughout the respiratory tract, and subsequent intracellular markers of bronchial epithelial cell response, plus application of this information to specific toxins of concern to the U.S. Air Force and Navy. These studies are organized into two coupled efforts: 1. prediction of the concentration distribution of inhaled agents within the bronchial tree (human and small animal models) via computational simulation and experimental measurement of bronchial airflow convection patterns and the resultant aerosol propagation; plus 2. bronchial epithelial cell response (gene expression, quantitative cell morphology, protein excretion and cell surface markers of inflammation) to the local toxin concentration exposures predicted in part 1. Although these efforts are aimed toward general understanding of any inhaled gaseous and particulate toxin, we are specifically focused toward the potential of inhaled hydrazine and trichloroethylene gases (or as vapor aerosols) plus combustion product inhalation of fine particulate aerosols as potential bronchial carcinogens. In addition, we have initiated studies to evaluate the mechanisms of bronchial wall inflammation after smoke inhalation and the potential reasons for the high variation of systemic absorption of combustion products that are engendered through stimulation of regional pulmonary vasoreactivity.

Each of the molecular biological studies incorporate the local bronchial concentration dependence predicted by the aerosol dispersion analysis. The ultimate goal is to produce computational methods that can accurately predict *in vivo* inhaled toxin dispersion in the lungs of humans and animals. These methods are aimed toward describing the concentration-time exposures of regional respiratory epithelial cells plus predict the efficiency of systemic absorption for a wide variety of potentially toxic materials. These predictions then allow for more realistic cellular exposure experiments after biochemical and morphometric markers of toxin responses allow for sampling and analysis of the respiratory tract at specific locations characteristic of differing toxin exposures. It is hoped the

predictions of inhalation dispersion, analysis of bronchial epithelial cellular markers, and methods of bronchial sampling after human or animal inhalation exposures can be applied to a wide variety of potential inhalation toxins in the future.

### **PROGRAM 1. Dispersion of Aerosol and Gaseous Toxins Throughout the Tracheobronchial Tree**

As opposed to internal organ toxicity where a ubiquitous toxic exposure over relatively slow time constants is assumed, the respiratory tract can experience focused concentration of inhaled toxins for variable periods. The bronchial tree, being a highly efficient particle filter and soluble gas scrubber is designed to remove potentially harmful inhalants within the cascade of bronchial airways. This function may create accumulations of toxic substances at focal locations within the airways. In addition, the bronchial network can actively reorient the airstreams to divert irritants away from zones where focused irritants induce bronchoreactivity. The complexities of this system have to date only allowed only a general understanding of where materials accumulate in the respiratory tract and, as such, the specific concentration and duration of bronchial toxic exposure cannot be accurately determined. These constraints markedly limit understanding of inhalation injuries, for both inflammatory responses to inhaled injuries (as exemplified by bronchiolitis after smoke inhalation) and bronchial carcinogenesis.

Predicting the concentration distribution of toxins in the respiratory tract has been a subject of study for many years but with limited success. Recently, two important features of this phenomenon have been advanced affording a much better understanding of the bronchial particle filtering and gaseous scrubbing systems. Understanding of bronchial tree morphometry, especially for those geometrical features which influence airway aerodynamics, has been advanced. Such advancements have stimulated understanding of the unique air convective patterns within the airways characteristic to each zone of the bronchial tree. Current technology, using very large computer facilities, may allow application of the descriptions for each individual bronchial airstream into large arrays to simulate the entire bronchial network's function. Such simulation of the convective airstreams can then be used to predict gas dispersion plus aerosol propagation and deposition in the lung. Toxin deposition in the airways, when further coupled with mucus, lymphatic, and cough clearance from the airways, then predicts the toxin concentration-time exposures to the bronchial epithelial cells. We have initiated a comprehensive, multi-disciplinary effort to better understand the mechanisms of aerosol and gaseous distribution to the airway mucosa.

Three zones of the tracheobronchial tree are under investigation. Cast models of human and small animal upper and central airways have been produced and measures of airway flow mechanics obtained. These measures include air flow velocity fields and turbulence characteristics (kinetic energy and frequency spectra) throughout the upper and central airways. Using these empirical velocity patterns and turbulence characteristics, computational simulations of particle behavior and gaseous dispersions in the upper observed and central airways are in process.

Characterization of gas and particle dispersion in the bronchial network distal to the lobar bronchi presents a more challenging problem in that direct empirical measures of flow within the tiny airways is impossible. Fortunately, the bronchial tree has a complex but defined morphometry such that flow studies can be carried out in large scaled models of the small airways under conditions of fluid

dynamic similitude (same ratio of forces acting on the flow). To date, empirical flow studies done in airway models carefully mimicking the mid and small bronchi and bronchioles have been initiated. In addition, computer (numerical solutions) simulations of bronchial airway flow and aerosol conductance are under development using empirical measures from the upper and central airway casts (to predict aerosol conductance through the central airways) and impregnating this on the computer simulation of aerosol conductance and deposition throughout the lung. In vivo experiments to justify these predictions are also underway using tagged aerosols in small animal models. In addition, predictions of gaseous dispersion throughout the human tracheobronchial are being developed. The predictions will be similar to the predictions of aerosol conductance except that molecular diffusion of the convecting gas is added to the analysis. In vivo human experiments are underway to evaluate these predictions, measuring the dispersion of SF<sub>6</sub> and Helium between the pharynx and segmented bronchi plus from segmented bronchi to alveoli in several segments of normal human subjects.

This study is aimed at predicting the dispersion of gases and aerosols throughout the tracheobronchial tree, understanding the mechanism influencing this distribution, and evaluating the predictions through application to the in vivo human and small animal.

#### **PROGRAM 2A. Gene Expression Related to the Metabolism of Toxins**

Although two people may be exposed to the same toxin such as hydrazine or trichloroethylene, the risks each encounters due to the exposure may differ. In order to better assess these interindividual risks, we are evaluating the expression of genes that function in the metabolism of such toxins. Currently we are studying the expression of genes for xenobiotic metabolism enzymes in human bronchial epithelial cells. These cells are obtained from normal volunteers by bronchial brush biopsy. RNA from these cells is extracted using Tri-Reagent (Molecular Research Center, Inc.). Reverse transcription using oligo dT primers and murine reverse transcriptase is performed in order to obtain cDNA from the messenger RNAs present in the cells. Once cDNA is obtained, a recently developed technique known as multiplex competitive polymerase chain reaction (Apostolakis, *et al.*, 1993, Anal. BioChem. 213, 277-284) is applied to determine the levels of gene expression. This technique involves the use of a competitive template (CT) during PCR so that a ratio of CT to native gene product can be obtained. This ratio allows for better detection of expression because it remains constant even if the polymerase chain reaction reaches a plateau. In addition, a housekeeping gene is always amplified in multiplex with the gene of interest. This controls for the amount of cDNA loaded in each tube. Routine application of both of these controls makes this method both highly sensitive and reproducible.

Over the initial three months of this project, we have synthesized primers for amplification of the native gene products and for the preparation of the native competitive templates of nine xenobiotic metabolism enzyme genes. A list of these genes, primers, and the lengths of both the native product and CT is found in Table 1. Prior to completion of synthesis of all of the competitive templates for the xenobiotic enzyme genes, we initiated evaluation of bronchial brush cells and alveolar macrophages from volunteers using a semi-quantitative method that included amplification of the native and CT of the housekeeping gene (-actin) and the native, but not the CT of the xenobiotic metabolism enzyme gene. This semi-quantitative method was used to evaluate expression of epoxide hydrolase (EH), phenol sulfotransferase (PST), N-acetyl transferase 1 (NATA1), N-acetyl transferase 2 (NATA2),

cytochrome p450 2F1 (CYP2F1), and cytochrome p450 2B7 (CYP2B7) in the bronchial epithelia cells from one volunteer. All of these genes were expressed. The relative amount of expression (in parentheses) using that of CYP2B7 as a standard equal to 1 was CYP2F1 (1.4 X), NAT1 (0.7 X), NAT2 (0.09 X), EH (0.97 X), and PST (0.97 X).

Most of the CT's have now been prepared. We will proceed with full multiplex competitive RT-PCR measurement of gene expression in additional volunteers and with other genes involved with the metabolism of toxins including those that may be found in products of combustion and in industrial air. We will sample human bronchial epithelial cells from a series of selected locations within the central bronchi and distal bronchioles. The sites will be selected to represent the spectrum of inhalation exposures predicted by our simultaneous aerosol and gaseous dispersion analysis. We expect to evaluate a total of 15 to 20 normal volunteers over the next year. In future years, we will seek to evaluate individuals with known exposure or risk for exposure to inhaled toxins.

GENE	NATIVE	CT	UPPER PRIMER SEQUENCE	POSITION
CYP1A1	355 bp	248 bp	5 <sup>1</sup> CAT CCC CCA CAG CAC AAC AAG 3 <sup>1</sup>	1241
CYP2B7	352 bp	248 bp	5 <sup>1</sup> GGA ACT TCG GAA ATC CAA GG 3 <sup>1</sup>	471
CYP2E1	338 bp	243 bp	5 <sup>1</sup> TCG GCA TGG GGT TGG AGT TGT 3 <sup>1</sup>	1003
CYP2F1	362 bp	284 bp	5 <sup>1</sup> GGG GAA GAG AAG CAT TGA GG 3 <sup>1</sup>	466
CYP3A4	373 bp	229 bp	5 <sup>1</sup> TTG CTG GCT GAG GTG GTT GGG 3 <sup>1</sup>	24
EH	351 bp	258 bp	5 <sup>1</sup> GGG TGA GAA CGT GGA GCC TG 3 <sup>1</sup>	31
NATA1	374 bp	275 bp	5 <sup>1</sup> TAA GAG ATT CGC AGA GGC AAC CTG 3 <sup>1</sup>	113
NATA2	372 bp	271 bp	5 <sup>1</sup> CTC CAA GGC CAC TGT TAG TTG TCA GA 3 <sup>1</sup>	17
PHENOL ST	349 bp	240 bp	5 <sup>1</sup> CCG AAA TGC AAA GGA TGT GGT 3 <sup>1</sup>	440

GENE	NATIVE	CT	LOWER PRIMER SEQUENCE	POSITION
CYP1A1	355 bp	248 bp	5 <sup>1</sup> ACA GCA GGC ATG CTT CAT GGT 3 <sup>1</sup>	1575
CYP2B7	352 bp	248 bp	5 <sup>1</sup> CCA TGT GGA GCAGGT AGG TG 3 <sup>1</sup>	803
CYP2E1	338 bp	243 bp	5 <sup>1</sup> AAT BCC CTC TTG CTA CTC GTC 3 <sup>1</sup>	1320
CYP2F1	362 bp	284 bp	5 <sup>1</sup> GCC TGG TGG TCG TGG ACG CT 3 <sup>1</sup>	808
CYP3A4	373 bp	229 bp	5 <sup>1</sup> CTC TGC TAT GCA TCC TCC TGA 3 <sup>1</sup>	376
EH	351 bp	258 bp	5 <sup>1</sup> GGG TGA AAC GGA ACT TAT CG 3 <sup>1</sup>	362
NATA1	374 bp	275 bp	5 <sup>1</sup> GTG TCT GAC CTC CCT TTC CAT TAT 3 <sup>1</sup>	463
NATA2	372 bp	271 bp	5 <sup>1</sup> ATA TTT TAA TGG GAG TTG AAG GGA CA 3 <sup>1</sup>	363
PHENOL ST	349 bp	240 bp	5 <sup>1</sup> GTG GGG ATG GTT GTG TAG TTA 3 <sup>1</sup>	768

GENE	NATIVE	CT	CT-PRIMER SEQUENCE	POSITION
CYP1A1	355 bp	248 bp	5 <sup>1</sup> ACA GCA GGC ATG CTT CAT GGG TCT CAC CGA TAC ACT TCC G 3 <sup>1</sup>	1447
CYP2B7	352 bp	248 bp	5 <sup>1</sup> CCA TGT GGA GCA GGT AGG TGGTGT GCC CCA GGA AAG TATT 3 <sup>1</sup>	679
CYP2E1	338 bp	243 bp	5 <sup>1</sup> AAT GCC CTCTTG CTA CTC GTC CTG GTG AGG ATG GAG TTG GAC 3 <sup>1</sup>	1204
CYP2F1	362 bp	284 bp	5 <sup>1</sup> GCC TGG TGG TCG TGG ACG CTC GGG AAT CTG GGG TCT AGGA 3 <sup>1</sup>	710
CYP3A4	373 bp	229 bp	5 <sup>1</sup> CTC TGC TAT GCA TCC TTC TGA GCT GAT GGC TTG GTG GAA TAG 3 <sup>1</sup>	211
EH	351 bp	258 bp	5 <sup>1</sup> GGG TGA AAC GGA ACT TAT CGG CCC CCA CCA CCC ATC TTC AA 3 <sup>1</sup>	248
NATA1	374 bp	275 bp	5 <sup>1</sup> GTG TCT GAC CTC CCT TTC CAT TATCCC ACT TTC AAA GTA CAC TGCAAA T 3 <sup>1</sup>	339
NATA2	372 bp	271 bp	5 <sup>1</sup> ATA TTT TAA TGG GAG TTG AAG GGA CA CAC TGA ATT CAA ACA AGG RGG TTA AA 3 <sup>1</sup>	236
PHENOL ST	349 bp	240 bp	5 <sup>1</sup> GTG GGG ATG GTT GTG TAG TTA CCT TTT GGG GTT CTC CTT TAT 3 <sup>1</sup>	639

## **PROGRAM 2B. Bronchial Inflammatory Mediators of the Inhalation Injuries**

We are developing molecular biological assessments of inflammatory indicators within the airway walls of small animals after exposure to hydrazine, trichloroethylene, and smoke inhalations from various combustions. The aim of this study is to enhance the understanding of the inflammatory pathways and develop cellular markers for the degree and persistence of inflammation as a function of the local airway dose-response and time-response of above described toxic chemicals. This effort will be extended to incorporate bronchoscopic airway samples obtained at bronchoscopy from humans exposed to low levels of hydrazine and trichloroethylene and smoke condensate in association with the gene expression studies described in 2A.

Our laboratory has extensive experience in the culture of ocular lens epithelial cells and regulation of gene expression of basement membrane molecules (collagenous and noncollagenous proteins) and their integrin receptors on exposure of epithelial cells to hormones, growth factors and cytokines (current NIH Eye Institute Study). These techniques have been extended to the bronchial epithelial cell analysis.

Epithelial damage in the airways is believed to be caused, in part, by the interaction of epithelial cells with leukocytes. Leukocytes must first adhere to and migrate through the endothelium, basement membranes, and epithelium before reaching the bronchial lumen. Adhesion molecules are important in this interaction and are upregulated or induced during an acute inflammatory reaction. The expression and modulation by hydrazine, trichloroethylene, and smoke inhalation on adhesion molecules ICAM-1, LFA-3, and CD44 will be investigated in human and animal bronchial epithelial cells. Retinoids,

glucocorticoids, transforming growth factors, and cytokines (TNF,IL-1) are also recognized to affect airway epithelial cells and will also be analyzed after exposure.

In a simultaneous experiment, we will also investigate the regulatory mechanisms of gene expression of basement membrane components (collagenous and noncollagenous proteins) in bronchial tissues or epithelial cells on exposure to above described toxins.

#### **PROGRAM 2C. Pulmonary Microvascular Vasoreactivity in Relation to Systemic Absorption of Inhaled Toxins**

Under this specific focus, we have initiated studies toward understanding the variation of systemic absorption of combustion products within smoke inhalation. We will investigate alterations of microvascular vasoreactivity as directed by the pulmonary macro- and microvascular endothelial cells. We will use a technique developed in our laboratory of assessing the output of vasoactive substances of endothelial cells in culture under a standard stimulus of graded hypoxia (16%,8% O<sub>2</sub>) with graded fluid shear stresses (high, medium, low flow states at the level of the precapillary arteriole).

Endothelial cells isolated from normal human pulmonary artery large vessel and microvascular sites are currently being propagated in culture. Measurements of the directed vasoreactivity of these cells will be examined via quantification of the release of endothelin -1 and 3 after hypoxia and shear. Quantitative multiplex competitive reverse transcriptase polymerase chain reaction (PCR) will be utilized to measure gene expression for endothelin which directly correlates to the levels of cytokine production. Once this model is established, several levels of endothelin release will be compared in the cells before and after exposure to LD<sub>50</sub> doses of hydrazine, trichloroethylene, and smoke representative of that inhaled from a class 1 fire.

Upon conclusion of this phase of testing, an animal model will be developed which will produce the above mentioned physiological conditions. The animals will be exposed to equivalent amounts of hydrazine, trichloroethylene, and smoke. Endothelial cells will be recovered from the pulmonary tract of the animal through the use of ULEX europeans 1 coated Dynabeads™ in the methods described by Jackson *et. al.* PCR can again be used to determine from recovered endothelium the expression of endothelin -1 and 3.

## **ARCHITECTURAL PROGRAM FOR THE BUILDING TO HOUSE THE CENTER FOR ENVIRONMENTAL MEDICINE**

Requests for an architectural firm to assist the Medical College of Ohio with the programming of the Center for Environmental Medicine were distributed in the July 19, 1994 issue of The Ohio Register. The Register was prepared and distributed from the State Architect's Office in Columbus, Ohio. This document is distributed to over 1,500 architectural and engineering firms that register with the State Architect's Office. Fifteen firms responded by submitting their qualifications for consideration. Four of the fifteen firms were selected for interviews, these four were selected based on a pre-determined rating form.

The interview committee was made-up of the following:

Michael Pereira, Ph.D., Professor of Pathology, Director, Center for Environmental Medicine  
Dan E. Olson, M.D., Ph.D., Professor of Medicine, Physiology/Biophysics; Chief,  
Pulmonary/Critical Care Medicine  
R. Douglas Wilkerson, Ph.D., Associate Vice President for Research and Grants Administration,  
Professor, Department of Pharmacology  
J. Michael Porter, Associate Vice President for Governmental Affairs and Community Service  
Sanford Taylor, Jr., Associate Vice President for Advanced Technology Development

All else being equal, the committee would have preferred to use a local firm. However, Payette Associates, Inc., of Boston, Massachusetts was selected because of their specific experience in programming and designing research laboratories, medical facilities and educational institutions.

The document developed by Payette Associates, Inc. has provided MCO with the necessary program information to determine the appropriate site, space needs, design criteria, and projected costs for the project. The report also provides details of spaces which will be needed in the new facility as well as advice on how to keep the space as flexible as possible. This document is included as Appendix 2.

**APPENDIX 1**

**Biographical Sketches for Key Personnel  
of the  
Center for Environmental Medicine**



## BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME Michael A. Pereira	POSITION TITLE Professor		
EDUCATION (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Ohio State University, Columbus, OH	B.S.	1967	MICROBIOLOGY
Ohio State University, Columbus, OH	PH.D.	1971	PHARMACOLOGY

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

### Professional Experience:

- 1971 - 1973 Damon Runyon Cancer Research Fellow, Supervisor: Dr. Richard W. Hendler, National Institutes of Health, National Heart and Lung Institute, Bethesda, Maryland 20014.
- 1973 - 1975 Research Associate, New York Blood Center, Coagulation Laboratory, 210 East 67th Street, New York, New York 10021.
- 1975 - 1978 Associate Research Scientist, New York University Medical Center, Department of Environmental Medicine, Tuxedo, New York 10987.
- 1978 - 1986 Supervisory Pharmacologist/Chief, Bioassay Branch, Toxicological and Microbiological Division, Health Effects Research Laboratory, U. S. Environmental Protection Agency, Cincinnati, Ohio 45268.
- 1986 - 1994 Vice President of Toxicology, Environmental Health Research and Testing, Inc., Cincinnati, Ohio 45245.
- 1994 - Present Professor, Department of Pathology and Director, Center for Environmental Medicine, Medical College of Ohio, Toledo, OH

### Honors and Awards:

- 1991 - Present NCI - Special Study Section - Z.
- 1988 - 1990 Society of Toxicology, Carcinogenesis Specialty Section Councilor.
- 1988 - 1993 Society of Toxicology, Secretary-Treasurer  
Member of American Association Cancer Research, Environmental Mutagen Society, American College of Toxicology, Society of Toxicology, American Society Pharmacology Experimental Therapeutics.

### Bibliography:

- Pereira, M. A. and Bull, R. J. Assessment of health risks associated with hazardous dump sites. IN: Proceedings of National Conference on Hazardous and Toxic Waste Management. (Eds. S. W. Liskowitz and A. J. Perna) New Jersey, Institute of Technology, N. J., pp. 98-106, 1980.

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- Allen, J.W., Stoner, G.D., Pereira, M.A., Backer, L.C., Sharief, U., Hatch, G.G., Campbell, J.A., Stead, A.G. and Nesnow, S. (1986). Tumorigenesis and Genotoxicity of Ethyl Carbamate and Vinyl Carbamate in Rodent Cells. Cancer Research, **46**: 4911-4915.
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- Herren-Freund, S.L., Pereira, M.A., Khoury, M.D., and Olson, G. (1987). The Carcinogenicity of trichloroethylene and its metabolites, trichloroacetic acid and dichloroacetic acid in mouse liver. Toxicol. Appl. Pharmacol., **90**: 183-189.
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### BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME William T. Gunning		POSITION TITLE Assistant Professor	
EDUCATION (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Medical College of Ohio, Toledo, Ohio	PH.D.	1991	PATHOLOGY
Bowling Green State University, Bowling Green, Ohio	MASTERS	1980	CELL BIOLOGY
Bowling Green State University, Bowling Green, Ohio	B.S.	1973	BIOLOGY

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

#### Professional Experience:

1974-1975	Histotechnologist, Department of Pathology, Medical College of Ohio
1975-1991	Supervisor, Electron Microscopy Laboratory, Department of Pathology, Medical College of Ohio
1991-Present	Assistant Professor of Pathology, Department of Pathology, Medical College of Ohio
1991-Present	Director, Electron Microscopy Laboratory, Department of Pathology, Medical College of Ohio

#### Bibliography:

1. Stoner, G.D., Babcock, M.S., Cathern, G.A., Klaunig, J.E., Gunning, W.T. and Knipe, S.M. *In vitro* Transformation of Rat Esophageal Epithelial Cells with N-nitrosobenzylmethylamine. *Carcinogenesis* 3(6):629-634, 1982.
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7. Gunning, W.T., Castonguay, A., Goldblatt, P.J., and Stoner, G.D. Strain A/J Mouse Lung Adenoma Growth Patterns Vary When Induced by Different Carcinogens. *Toxicologic Pathol.* 19(2):168-175, 1991.

## Biographical Sketch

William T. Gunning

Page 2

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10. You, M., Wang, Y., Lineen, A.M., Gunning, W., Stoner, G.D. and Anderson, M.W. Mutagenesis of K-ras Protooncogene by N-Ethyl-N-Nitrosourea and Diethylnitrosamine During Initiation of Mouse Lung Tumorigenesis. *Carcinogenesis*, Vol. 13(9):1583-1586, 1992.
11. Matzinger, S.A., Gunning, W.T., You, M. and Catonguay, A. K-ras Mutations in NNK-Initiated and BHT-Promoted Lung Tumors in A/J Mice. *Molecular Carcinogenesis*, in press.

## BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME James A. Hampton, Ph.D.	POSITION TITLE Assist. Professor of Pathology and Urology		
EDUCATION ( <i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.</i> )			
INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Ohio University, Athens, OH	B.S.	1970	Mathematics
West Virginia University, Morgantown, WV	Ph.D.	1985	Anatomy

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

### Professional Experience:

- 1984-86      Postdoctoral Fellow, Department of Pathology, Medical College of Ohio, Toledo, OH
- 1986-1988    Instructor in Pathology, Department of Pathology, Medical College of Ohio, Toledo, OH
- 1988-92      Research Assistant Professor, Department of Pathology, Medical College of Ohio, Toledo, OH
- 1992-Present Assistant Professor, Departments of Pathology and Urology, Department of Pathology, Medical College of Ohio, Toledo, OH

### REPRESENTATIVE PUBLICATIONS (out of 31)

- Khan, N.A., **Hampton**, J.A., Lacher, D.A., Rapp, J.P., Gohara, A.F., and Goldblatt, P.J.: Morphometric evaluation of the renal arterial system of Dahl salt-sensitive and salt-resistant rats on a high salt diet. I. Interlobar and arcuate arteries. *Lab. Invest.* 57:714-723, 1987.
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- Selman, S.H., **Hampton**, J.A., Morgan, A.R., Keck, R.W., Balkany, A.D., and Skalkos, D.: Copper benzochlorin, a novel photosensitizer for photodynamic therapy: Effects on a transplantable urothelial tumor. *Photochem. Photobiol.* 57:681-685, 1993.
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- Slaton, J., Hampton, J.A., and Selman, S.H.: Exposure to alkyl-lysophospholipids inhibits in vitro invasion of transitional cell carcinoma. *J. Urol.*, (in press).
- Henning, J.P., Fournier, R.L., and **Hampton**, J.A.: A transient mathematical model of oxygen depletion during photodynamic therapy. *Radiation Res.* (submitted)
- Feyes, D.K., Morgan, A.R., Garbo, G.M. and **Hampton**, J.A.: In vitro photosensitization of cells with tin (IV) ethyl etiopurpurin dichloride. *Photochem. Photobiol.* (submitted).

## BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME Yian Wang	POSITION TITLE Assistant Professor		
EDUCATION ( <i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.</i> )			
INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Beijing Medical College Beijing, China	B.S./M.D.	1982	MEDICINE
Medical College of Ohio, Toledo, Oh	Ph.D.	1990	PATHOLOGY

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

### Professional Experience:

- 1993 - Present      Assistant Professor, Department of Pathology, Medical College of Ohio, Toledo, Ohio
- 1990 - 1992      Research Associate, Department of Medicine, Medical College of Ohio, Toledo, Ohio

### Honors and Awards:

- 1990 -      Dean's Award at Graduation, Medical College of Ohio
- 1990 -      Graduate Student Award from 29th Annual Meeting, Society of Toxicology, (Molecular Carcinogenesis Section)
- 1985-1990      Predoctoral Fellowship, Medical College of Ohio
- 1978-1982      Medical Student Fellowship, Beijing Medical College

### Bibliography:

- You, M., Wang, Y., Stoner, G.D., Maronpot, R.R., and Anderson, M.W. (1991). Activation of proto-oncogenes in mouse model systems. *Experimental Lung Research*, 17:3889-400.
- You, M., Wang, Y., Stoner, G.D., You, L., Maronpot, R.R., Reynolds, S.H., and Anderson, M.W. (1992). Parental bias of *K-ras* oncogenes detected in lung tumors from mouse hybrids. *Proc. Natl. Acad. Sci.* 89:5804-5808.
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## BIOGRAPHICAL SKETCH

NAME Dan E. Olson	POSITION TITLE Professor		
EDUCATION (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Colorado, Boulder	B.Sc.	1965	ENGINEERING
University of California, Berkeley		1967	PRE-MEDICINE
University of Colorado School of Medicine, Denver	M.D.	1969	M.D.
Imperial College of Science & Technology, University of London, London, England	Ph.D.	1972	BIOENGINEERING, PHYSIOLOGY

### Professional Experience:

1969-1972	Lecturer, Academic Visitor, Physiological Flow Studies Unit, Imperial College of Science and Technology, London, England
1978-1980	Clinical Assistant Professor, Department of Internal Medicine, University of Washington, Seattle, Washington
1980-1985	Assistant Professor, Department of Internal Medicine, Department of Bioengineering, University of Michigan, Ann Arbor, Michigan
1985-1991	Associate Professor, Department of Internal Medicine, University of Kansas School of Medicine, Wichita, Kansas
1986-1993	Adjunct Professor, College of Engineering, College of Health Sciences, Wichita State University, Wichita, Kansas
1991-1993	Professor of Internal Medicine, University of Kansas School of Medicine, Wichita, Kansas
1993-	Professor, Department of Mechanical Engineering (Bioengineering), University of Toledo, Toledo, Ohio
1993-	Professor, Department of Internal Medicine, Department of Physiology/Biophysics, Medical College of Ohio, Toledo, Ohio

### Honors and Awards:

1961-1965	Medio J. Bacco Memorial Scholarship, Michigan
1967-1973	University of Colorado Medical School, Special Physiology Award, Boettcher Foundation Medical Scholarship, Colorado Medical Society Scholarship, Glen Cheney Scholarship, Health Profession Scholarship
1966-1968	National Institutes of Health, Predoctoral Research Fellowship, Young Investigators Research Award
1969-1972	American Thoracic Society Fellowship
1982-1984	University of Michigan, Faculty Teaching Award; Pulmonary Medicine best paper with associate member, ACP Regional Meetings
1989-1993	University of Kansas, best paper with associate member, ACP Regional Meetings; best paper with associate member, ACP National Meetings; Faculty Teaching Award, Internal Medicine-Wichita; The Chancellors Club

### Bibliography:

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2. Hammersley, J.R., Olson, D.E., Snyder, B.: Inspiratory flow development in small airways. J. Appl. Physiol., accepted, 1993.



3. Hammersley, J.R., Olson, D.E., Snyder, B.: Expiratory flow development in small airways. *J. Appl. Physiol.*, accepted 1993.
4. Hammersley, J.R. and Olson, D.E.: Physical models of the smaller pulmonary airways. *J. Appl. Physiol.*, 72(6):2402-2414, 1992.
5. Beachey, W.D. and Olson, D.E. Quantifying ventilatory reserve to predict respiratory failure in exacerbations of COPD. *Chest* 97(5):1086-1091, 1990.
6. Snyder, B. And Olson, D.E.: Flow development in a modal airway bronchus. *J. Fluid Mechanics* 207:379-391, 1989.
7. Snyder, B., Olson, D.E., Hammersley, J.R., Peterson, C.V. Jr., and Jaeger, M.J.: Reversible and irreversible components of central-airway flow resistance. *J. Biomech. Eng.* 109(2):154-159, 1987.
8. DeTullio, P.L., Kitking, D.M., Arslanian, C., and Olson, D.E.: Compliance measure development and assessment of theophylline therapy in ambulatory patients. *J. Clin. Pharm. and Therapeutics* 12:19-26, 1987.
9. Geometric determinates of airflow distribution within the lung. *Advances in Bioengineering*, ASME Publication BED 2:66, 1986.
10. Snyder, B. And Olson, D.E.: Entrance-flow in variance in a tapering elliptical slit. *Physics of Fluids* 29(8):2341, 1986.
11. Olson, D.E., Snyder, B. and Hammersley, J.R.: Character of turbulence in the central airways. The proceedings of the Thirty-eighth Annual Conference on Engineering in Medicine and Biology, published in AEMB., 1985.
12. Olson, D.E., Snyder, B., Debler, W., and Hammersley, J.R.: Aerodynamic sound generation in small pulmonary airways. The proceedings of the Thirty-eighth Annual Conference on Engineering in Medicine and Biology, published in AEMB, 1985.
13. Snyder, B., Hammersley, J.R., and Olson, D.E.: The axial skew of flow in curved pipes. *J. Fluid Mech.* 161:281, 1985.
14. Olson, D.E. and Snyder, B.: The upstream scale of flow development in curved circular pipes. *J. Fluid Mech.* 150:139-1548, 1985.
15. Olson, D.E., Parker, K.H. and Snyder, B.: A pulsed wire probe for the measurement of velocity and flow direction in slowly moving air. *ASME J. Biomech. Eng.* 196(1):72-78, 1984.
16. Olson, D.E. and Snyder, B.: The growth of swirl in curved circular pipes. *Physics of Fluids* 26(2):347-349, 1983.
17. Stauffer, J.L., Olson, D.E. and Petty, T.L.: Complications and consequences of endotracheal intubation and tracheotomy: A prospective study of 150 critically ill adult patients. *Am. J. Fed.* 70:65-76, 1981.
18. Jackson, A.C. and Olson, D.E.: Comparison of direct acoustical area measurements in physical models of human central airways. *J. Appl. Physiol.* 48(5):896-902, 1980.
19. Pardee, N.E., Morgan, E.H., Winterbauer, R.H. and Olson, D.E.: Combinations of four physical signs as indicators of ventilatory abnormality in obstructive pulmonary syndromes. *Chest* 77(3):354-358, 1980.
20. Filley, G.P. and Olson, D.E.: The hyperpnea of exercise and chemical disequilibria. *Chest* 73:267, 1978.
21. Olson, D.E., Sudlow, M.F., Horsfield, K. and Filley, G.F.: The convective patterns of flow during inspiration in the upper and central airways. *Arch. Int. Med.* 131:51-37, 1973.
22. Olson, D.E.: Biofluid mechanics, (Guest lecture to the American Physical Societies 25th International Meeting of the Division of the Fluid Dynamics, November, 1972). *Physics of Fluids*, 1973.
23. Olson, D.E., Iliff, L.D. and Sudlow, M.F.: Some aspects of the physics of flow in the central airways. *Bull. Physiopathol. Respir.* 8:391-408, 1972.
24. Horsfield, K., Dart, G.A., Olson, D.E., Filley, G.F. and Cuming, G.: Models of the human bronchial tree. *J. Appl. Physiol.* 31(2):207-217, 1971.

## BIOGRAPHICAL SKETCH

NAME Jeffrey R. Hammersley		POSITION TITLE Associate Professor	
EDUCATION (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Michigan, Ann Arbor	B.S.	1972	ZOOLOGY
Wayne State University School of Medicine, Detroit	M.D.	1976	MEDICINE

### Professional Experience:

1982-1985      Instructor, Pulmonary Division, Department of Internal Medicine, University of Michigan, Ann Arbor, MI

1985-1988      Assistant Professor, Pulmonary/Critical Care Division, Department of Internal Medicine, University of Michigan Medical School, Ann Arbor, MI

1988-1994      Adjunct Assistant Professor, Fluid Mechanics, Instrumentation and Electronics Section, Graduate Institute of Technology, University of Arkansas at Little Rock

1988-1994      Assistant Professor, Pulmonary/Critical Care Division, Department of Internal Medicine, University of Arkansas for Medical Sciences

1994-          Associate Professor of Clinical Medicine, Physiology and Molecular Medicine, Pulmonary/Critical Care Division, Department of Internal Medicine, Medical College of Ohio, Toledo, OH

### Honors and Awards:

Alpha Omega Alpha Society (Junior year)

American Lung Association Fellowship grant, 1980-81 (University of Michigan)

Red Sash Award UAMS 1993

### Bibliography:

Grismer, J.T., Hart, J.K., San Pedro, G.S., Hammersley, J.R.: Introduction of a computer-based patient assessment expert system into the junior clerkship rotation - A three year experience of problems and solutions (submitted to Journal of Surgical Education).

Hammersley, J.R., Olson, D.E.: Physical models of the smaller pulmonary airways. J. Appl. Physiol. 72:2402-2414, 1992.

Hammersley, J.R., Reddy, R.N., Arabshahi, A.: Computational simulation of airflow within human lungs. Proceedings of the 1992 Arkansas computer conference, Little Rock, AR, 1992.

Hammersley, J.R., Grum, C.M., Green, R.A.: The correlation of subcarinal density visualized on plain chest radiographs with computed tomography scans. Chest, 97:869-872, 1990.

Hammersley, J.R., Cooney, K.: Evaluating the utility of differential diagnosis systems. Proceedings of the Twelfth Annual Symposium on Computer Applications in Medical Care. IEEE Computer Society Press, 229-231, 1988.

Hammersley, J.R., Ragu, G., Sabesin, S.M.: Simultaneous use of theophylline and H<sub>2</sub> receptor antagonists in patients with ulcer disease. Advances in Therapy 4(5), 1987.

Snyder, B., Olson, D.E., Hammersley, J.R.: Reversible and irreversible components of central airways flow resistance. ASME Journal of Biomechanical Engineering 109:154-159, 1987.

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- Olson, D.E., Snyder, B., Hammersley, J.R.: character of turbulence in the central airways. Proceedings of 38th Conference on Engineering in Medicine and Biology, AEMB, 1985.
- Schwartz, D.B., Beals, T.F., Wimbish, K.J., Hammersley, J.R.: Transbronchial fine needle aspiration of bronchogenic cysts. Chest 88:(4):573-575, 1985.
- Snyder, B., Hammersley, J.R., Olson, D.E.: the axial skew of flow in curved pipes. J. of Fluid Mechanics 161:281-294, 1985.
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## BIOGRAPHICAL SKETCH

NAME Rajinder s. Sawhney		POSITION TITLE Associate Professor	
EDUCATION <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Jammu University, India	PH.D.	1970	CHEMISTRY

### Professional Experience:

1964 - 1978	Scientist, Regional Research Laboratory, Council of Scientific and Industrial Research, Government of India, Jammu-Tawi, India
1967 - 1968	Visiting Scientist, Commonwealth Scientific and Industrial Research Organization, Division of Organic Chemistry, Melbourne, Australia
1977 - 1978	Visiting Scientist, Department of Chemistry, University of Georgia, Athens, GA
1975 - 1977	Visiting Scientist, Department of Biochemistry, University of Tennessee, Memphis, TN
1978 - 1982	Research Associate, Department of Biochemistry, University of Tennessee, Memphis, TN
1982 - 1985	Research Assistant Professor, Department of Oral Biology, Northwestern University, Chicago, IL
1985 - 1994	Assistant Professor, Department of Biochemistry, Rush -Presbyterian-St. Luke's Medical Center, Rush Medical, College, Chicago, IL
1988 - 1994	Assistant Professor, Department of Medicine, Rush Medical College, Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL
1994 -	Associate Professor, Medical College of Ohio, Department of Pulmonary Medicine, Toledo, OH

### Honors and Awards:

1976	Recipient of American Cancer Society Award, Memphis, TN
1982	Recipient of American Cancer Society Award, Memphis, TN
1985 - 1986	Recipient of Rush Committee on Reseach Grant Award
1985 - 1986	Recipient of Young Investigator Research Award, American Diabetes Association, Chicago, IL
1986 - 1987	Recipient of NIH Small Grant Award
1990 - 1995	Reciepoint of NIH RO-1 Grant Award
1993	Co-Investigator in Anchored Cell Analysis and Sorting Cytometer (ACAS 570) Shared Instrument Grant, funded by NIH. Principal Investigator: David Rubin, M.D.
1993 - 1998	Collarobator in Cellular Biochemistry Core of SCOR Grant, Funded by NIH. Principal Investigator: Dr. Klaus E. Kuettner.
1994	Grant application (RO1) to NIH for competition, renewal pending.

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3. Sawhney, R.S. and Silber, I.E. SPARC gene expression by anterior lens capsule epithelial cells and its regulation by Retinoic acid, 1994 (in preparation)
4. Sawhney, R.S. and Bone, R.C.: Endotoxin alters the expression of extracellular matrix proteins by cultured endothelial cells. Cell. Mol. Biol. Res. 39:589-599, 1993.
5. Sawhney, R.S. Expression of Type I and III Procollagen in Lens Epithelial Cells. Invest. Ophthalmol. Vis. Sci. 34:2195-2202, 1993.
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7. Sawhney, R.S., Hering, T.M., and Sandell, L.J.: Biosynthesis of Small Proteoglycan II (Decorin) by Chondrocytes and Evidence for a Procore Protein. J. Biol. Chem. 266:(14):9231-9240, 1991.
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14. Moore, J.F., Mody, N.V., Sawhney, R.S. and Pelletier, S.W.: Atidine  $C_{22}H_{23}NO_3$ . Cryst. Struct. Com. 8:649, 1979.
15. Pelletier, S.W., Mody, N.V., Sawhney, R.S.: Carbon-13 NMR spectra of some  $C_{19}$ -diterpenoids alkaloids and their derivatives. Can. J. Chem. 57:1652, 1979.
16. Mody, N.V., Sawhney, R.S. and Pelletier, S.W.: Carbon-13 NMR spectral assignments for pyrrolizidine alkaloids. J. Natl. Products 42:417, 1979.
17. Pelletier, S.W. and Sawhney, R.S.: Ajacusine and ajadine, two new diterpenoid alkaloids from *Delphinium ajacis*. Heterocycles 9:463, 1978.
18. Sharma, R.K. and Sawhney, R.S.: Metabolic regulation of steroidogenesis in isolated adrenal cell. Investigation of the ACTH Hormone, cGMP, and cAMP control step. Biochemistry 17:316, 1978.
19. Pelletier, S.W., Sawhney, R.S. and Mody, N.V.: Ambiguine and dihydroajaconine: two new diterpenoid alkaloids from *Consolida ambigua*. Heterocycles 7:327, 1977.
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21. Suri, K.A., Suri, O.P., Sawhney, R.S., Gupta, O.P. and Atal, C.K.: Preparation of pharmacodynamic compounds based on 1-methylene pyrrolizidine. Indian J. Chem. 15:B:972, 1977.

## BIOGRAPHICAL SKETCH

NAME Gouri Shanker	POSITION TITLE Instructor/Senior Research Associate		
EDUCATION (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Agra University, Nainital	M.S.	1968	ORGANIC CHEMISTRY
University of Bombay, Bombay, India	Ph.D.	1972	CHEMISTRY
University of Tennessee, Memphis, TN	Ph.D.	1968	BIOCHEMISTRY

### Professional Experience:

- 1987-1988      Assistant Member/Assistant Professor, Department of Neurobiology, Cornell Institute for Medical Research, University of Medicine and Dentistry of New Jersey (MDNJ), Camden, NJ
- 1988-1994      Assistant Professor, Department of Comparative Medicine, Bowman Gray School of Medicine, Winston-Salem, NC
- 1994            Instructor/Senior Research Associate, Medical College of Ohio, Department of Pulmonary Medicine, Toledo, OH

### Honors and Awards:

- 1993            Selected for 2nd edition of Marquis Who's Who in Science and Engineering
- 1992            Selected for listing in the International Brain Research Organization/World Federation of Neuroscientists Directory (IBRO)
- 1988            Selected for 2nd edition of Marquis Who's Who of Emerging Leaders in America
- 1987            Selected for 13th edition of Men of Achievement, International Biographical Center, Cambridge England
- 1986-1987      Selected for 21st edition of Marquis Who's Who in the Eastern USA
- 1979-1982      NIH Postdoctoral Fellow

### Bibliography:

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- Claro, E., Wallace, M.A., Fain, J.N., Nair, B.G., Patel, T.B., Shanker, G. And Baker, H.J. Modulation of phosphoinositide-specific phospholipase C and adenylyl cyclase of brain cortical membranes in feline GM<sub>1</sub> and GM<sub>2</sub> gangliosidosis. *Mol. Brain Res.* 11:265-271, 1991.
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9. Shanker, G. And Pieringer, R.A. Investigations on myelinogenesis *in vitro*: A. The occurrence of endogenous protein kinase and its role in the phosphorylation of myelin basic proteins in myelin-like membranes isolated from cerebral cell cultures. *Biosci. Rep.* 7:151-157, 1987.
10. Shanker, G., Campagnoni, A.T. and Peiringer, R.A. A developmental study of the estimation of myelin basic protein mRNA levels using 1.85 Kb MBP-cDNA probe. Regulation by thyroid hormone. *J. Neurosci. Res.* 17:220-224, 1987.
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13. Amur, S.G., Shanker, G., and Pieringer, R.A.  $\beta$ -adrenergic stimulation of protein (arginine) methyltransferase activity in cultured cerebral cells from embryonic mice. *J. Neurosci. Res.* 16:377-387, 1986.
14. Shanker, G. And Pieringer, R.A. Developmental study on the regulation of neurotransmitter-sensitive adenylate cyclase systems in primary cerebral cell cultures from embryonic mice. *Biosci. Rep.* 5:601-608, 1985.
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17. Amur, S.G., Shanker, G. And Pieringer, R.A. Regulation of myelin basic protein (arginine)methyltransferase by thyroid hormone in myelinogenic cultures of cells dissociated from embryonic mouse brain. *J. Neurochem.* 43:494-498, 1984.
18. Bhat, N.R., Shanker, G. And Pieringer, R.A. Cell proliferation in growing cultures of dissociated embryonic mouse brain: macromolecular and ornithine decarboxylase synthesis and regulation by hormones and drugs. *J. Neurosci. Res.* 10:221-230, 1983.
19. Shanker G., Bhat, N.R. and Pieringer, R.A. Investigations of myelination *in vitro*: thyroid hormone receptors in cultures of cells dissociated from embryonic mouse brain. *Biosci. Rep.* 1:289-297, 1981.
20. Shanker, G. and Sharma, R.K. Characterization of ectopic alpha-adrenergic binding receptors of adrenocortical carcinoma cells. *Endocrinology* 106:1594-1598, 1980.

## BIOGRAPHICAL SKETCH

NAME James C. Willey		POSITION TITLE Assistant Professor	
EDUCATION <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Vermont, Burlington	B.A.	1974	ZOOLOGY
Medical College of Ohio, Toledo	M.D.	1978	MEDICINE

### Professional Experience:

1979-1981	Resident, Internal Medicine, VA-Georgetown (Georgetown University and Veterans Administration Hospitals, Administered by VA Hospital), Washington, DC
1981-1984	Medical Staff Fellow, National Cancer Institute, Laboratory of Human Carcinogenesis, Bethesda, MD
1984-1986	Senior Staff Fellow, National Heart Lung Blood Institute, Pulmonary Branch, Bethesda, MD
1986-1988	Biotechnology Fellow, National Cancer Institute, Laboratory of Human Carcinogenesis, Bethesda, MD
1988-1990	Expert, National Cancer Institute, laboratory of Human Carcinogenesis, Bethesda, MD
1990-1994	Assistant Professor, Department of Environmental Medicine, University of Rochester School of Medicine and Dentistry, Rochester, NY
1994-	Associate Professor, Pulmonary Division, Department of Medicine, Medical College of Ohio, Toledo, OH

### Bibliography:

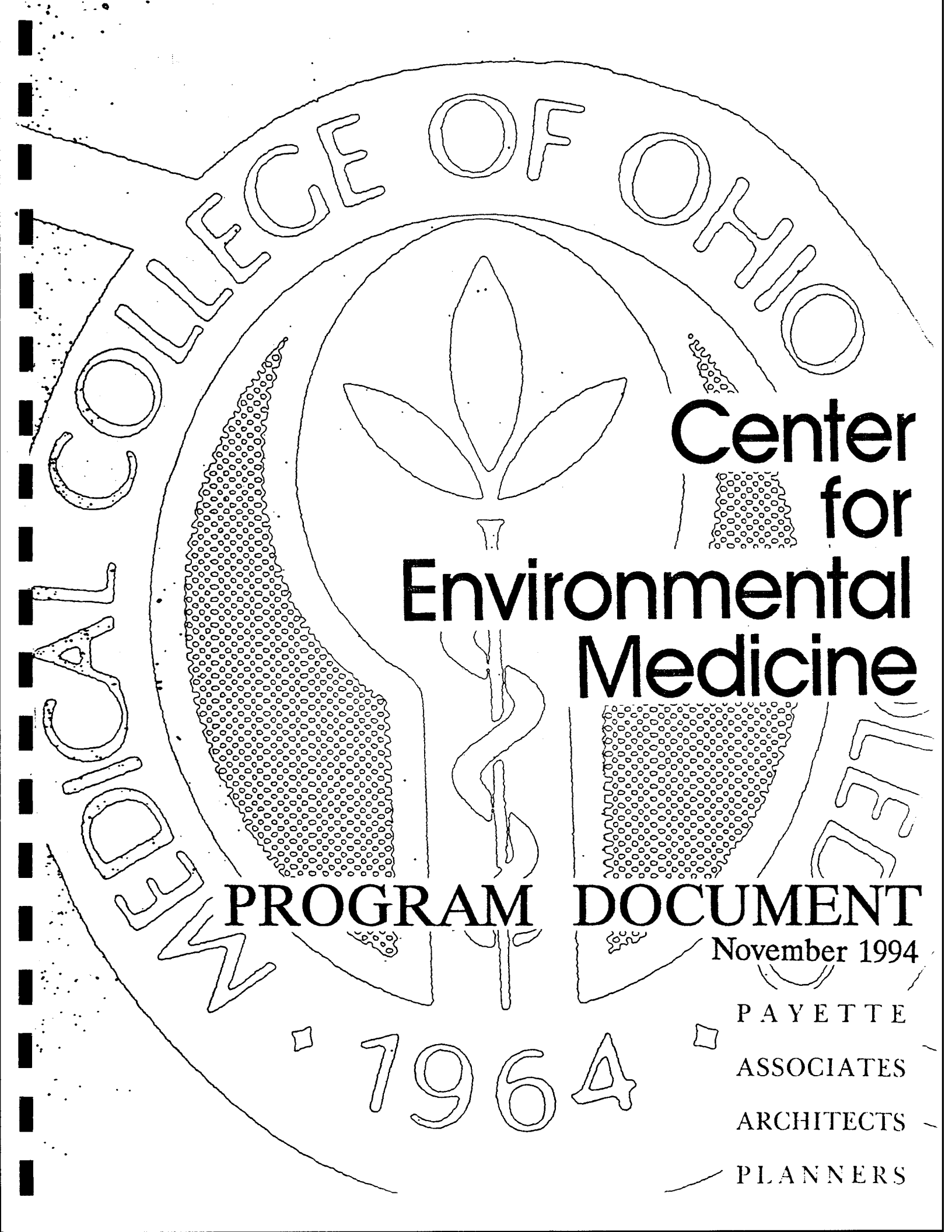
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## **APPENDIX 2**

### **Program Document for the Building for the Center for Environmental Medicine**



**Center  
for  
Environmental  
Medicine**

**PROGRAM**

**DOCUMENT**

November 1994

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MEDICAL COLLEGE OF OHIO  
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PROGRAM DOCUMENT

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TABLE OF CONTENTS

1. Executive Summary
2. Statement of Mission and Goals
3. Building Population and Projections
4. Building Concepts - Modularity
5. Program Summary Tabulation
6. Typical Room Diagrams
7. Site Evaluation
8. Engineering Systems Descriptions
9. Architectural Systems Outline
10. Budget Costs
11. Appendix  
Preliminary Space Summary with Investigators' Requests

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1. EXECUTIVE SUMMARY

This document defines and quantifies the physical characteristics of a proposed new building to house the Center for Environmental Medicine (CEM) at the Medical College of Ohio. The CEM was recently established in existing laboratory space with an initial grant which acquired certain items of equipment and recruited key individuals from MCO and elsewhere.

The Center's overall objective is to develop and validate methodologies for the assessment of human risks from toxic substances introduced by man into the environment. (See Statement of Mission and Goals - Part 2) Much of the science done in the CEM will be done with animal and human tissue at the cell and molecular level in the laboratories. Other work will be done using animal models in vivo and computer models of human physiological systems. Small amounts of toxic substances will be used, handled and disposed of in accordance with established practices. There will likely be work done in cooperation with the Department of Defense and the Air Force. The CEM will also act as an agent of technology transfer between MCO and the Northwest Ohio Advanced Technology Park (NOATP).

The proposed site for the Center for Environmental Medicine is on a southwest corner parcel of the NOATP campus. No other potential sites have been identified which satisfy the criteria of proximity to both MCO and NOATP campuses, contain adequate land area for future expansion, have immediate access to major roadways and identify the building's role in the community.

The space needs documented herein were determined in conversations with each of the investigators now associated with the CEM programs at MCO. Their individual space needs are documented in the Preliminary Space Summary in Part II.

The concept of modular spatial and systems organization described in Part 4 has proven to be the most important and lasting development in research laboratory design in the last two decades. A CEM building would not be ready for occupancy for at least two years. A CEM building will need to respond with flexibility to changes in research programs within the planning and construction period and for decades beyond its initial occupancy.

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Payette Associates has translated the investigators' individual space needs into the Modular Space Tabulation in part 5. In order to communicate the basis on which rooms were sized in the space tabulation and as an aid to using this program to develop building plans, room diagrams have been drawn for most typical spaces. These diagrams document furniture and other items discussed in the programming conversations with the investigators.

Section 10, Budget Costs, addresses the likely construction budget which will be required to realize this project. It was established from the experience of Payette Associates with similar laboratory projects nationwide together with the experience of local Toledo design and construction professionals.


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2. GOALS FOR CEM

MISSION STATEMENT

To develop a unique program to investigate the effects of hazardous substances in the environment on living human cells and tissue.

GOALS

- 
- 3 ■ Respond to new research initiatives over time; to reassign space while minimizing retrofitting costs.
  - 4 ■ A building which will facilitate and symbolize the transfer of technology from MCO to the Northeast Ohio Advanced Technology Park industries and the community at large.
  - 2 ■ Potential to conduct programs requiring security and confidentiality required by DOD and the AirForce.
  - 1. 2. ■ *a building which will respond to the research needs of DOD, the Air Force & M.C.O.*
  - 5 ■ Embody the design and construction standards for buildings in the Northeast Ohio Advanced Technology Park.
  - 6 ■ "All Under One Roof" concept (contain all support and core facilities necessary for molecular and cell biology environmental research).

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3. **BUILDING POPULATION AND PROJECTIONS**

The space needs tabulation which follows was developed through discussions with each of the principal investigators presently identified with the Center for Environmental Medicine programs already in place at MCO. These programs represent an initial research effort which is expected to expand into a comprehensive mission to study the effects of toxic substances in the environment for decades to come. The need to expand and recruit must, however, be balanced with the realities of potential funding sources for a new CEM building. Fortunately, the site can be designed to accommodate future building additions and the new CEM would be designed to anticipate that future expansion.

Part 10 of this program document contains budget construction costs. On the basis of those costs, a building reflected in the following needs tabulation represents a construction budget of about \$12,000,000. As described in part 4, BUILDING CONCEPTS - MODULARITY, this building would be designed to adapt to successive research teams and initiatives over time. But, at 53,000 GSF it will accommodate just the equivalent of the research programs now in place as they expect to expand within the next two to three years.



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4. DESIGN CONCEPT

Modular Organization

The stated goals of flexibility and adaptability are a direct response to the anticipated research diversity and the need to accommodate new research initiatives from year to year. A modular approach to space and benchwork allows changes to be made by re-using and rearranging standard benchwork elements within standard sized rooms. Such standardization allows the Medical College to offer predictable facilities to faculty members and also reduces the likelihood of excessive customization and therefore time and cost in recruitment and facilities adjustments. The modular approach is most often applied to the primary bench space in a facility, but can be applied to some support areas as well to maximize space utilization.

The module upon which this program has been based is 567 NSF - 21'-0" x 27'-0". It is shown in two internal layouts. Sketch No. 2 accommodates 4 researchers, each with an 8 foot bench and a desk. Sketch No. 3 accommodates 6 researchers, each with a 6 foot bench and a desk. The amount of equipment support space varies and would be enhanced by equipment rooms and other programmed spaces for each Principal Investigator's needs. A Principal Investigator would be assigned fractions or multiples of modular lab space for his primary lab team. Since the modular lab space is generic, it can be incrementally reassigned as one group grows and an adjacent group shrinks.

The laboratory bench and cabinetry is also conceived in a modular system of components: benchtops, cabinet units, shelf units, sink units. Cabinet units and standard length shelves can be moved within a lab or exchanged between labs as needed by the researchers themselves without the need for workmen or special tools. A pencil drawer can be converted to a keyboard tray, a left-handed pedestal to a right-handed location, an undercounter cabinet can make way for a knee-hole and its top be used to support a piece of benchtop equipment.

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Every lab module and most other support spaces in the building are served by mechanical and electrical services in a modular manor. Plumbing lines are isolated by valves and electrical services circuited so that each space can be shut down for work or modification without interrupting services to any other space. Where services are not initially required, pathways and valved stubs are provided for future services.

There are no structural "monuments" within the body of the building to impede spatial flexibility; duct shafts, shear walls, stairways and elevators are on the periphery and corridors are placed to allow universal access to all space. Exterior wall area is prioritized for windows so that all space where people work can have natural light and views. Corridor circulation is conceived as simple and a permanent perceptual organizing element of the building at every floor level.

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**5. PROGRAM SPACE SUMMARY**

<u>Sketch No.</u>	<u>Room</u>	<u>NSF</u>	<u>Qty.</u>	<u>Extension</u>
<b>ASSIGNED SPACE</b>				
2/3	Laboratory Modules	567	25	14,175
4	Faculty Offices	165	12	1,980
6	Group Offices - 4 desks	165	10	1,650
5	Tech. Offices	116	4	464
16	Storage/Fluorescence Microscope/ Small Darkroom, etc.	45	12	540
			Subtotal	18,809 NSF
<b>SHARED SPACE (Assume 2 lab floors)</b>				
7	Support Offices - 3 desks	250	2	500
13	Conference/Library Rooms	240	2	480
14	Process Darkrooms	130	2	260
15	Copier Nooks	24	2	48
17	Cold Rooms	115	2	230
17	Cold/Warm Rooms	115	2	230
18	Equipment Rooms	284	4	1,136
19	Autoclave Rooms (2 medium autoclaves)	160	2	320
20	Break Rooms with kitchenettes	200	2	400
			Subtotal	3,604 NSF

Each Floor will have:

- Appropriate Toilet Rooms
- Housekeeping Closet
- Electrical Room
- Data and Phone Room
- Tank Closet (Manifolded)

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<u>Sketch No.</u>	<u>Room</u>	<u>NSF</u>	<u>Qty.</u>	<u>Extension</u>
<b>CORE FACILITIES</b>				
<b>1. ELECTRON MICROSCOPY SUITE</b>				
21	E.M. Rooms 2 TEM Rooms 1 HR/FEG/BEI/EDS Room	180	3	540
--	Confocal Microscope Room	142	1	142
--	Office	80	1	80
--	Prep Room 1-6' chemical fume hood	115	1	115
--	Storage	60	1	60
--	Fine Section Room 4 stations sinks, workcounter	230	1	230
--	Small Conference Room	115	1	115
--	Darkrooms Sink, counter	50	3	150
--	Transformer Room	50	1	50
--	Copystand Room	115	1	115
			Subtotal	1,597 NSF
<b>2. CENTRAL DNA LAB</b>				
(1 module - see above) Synthesizer 1-5' chemical hood Tech. desk area				
<b>3. ANIMAL CARE FACILITY</b>				
27	Modular Cage Room 3 double-sided racks each	150	14	2,100
4	Office	165	1	165
28	Restrooms, Shower, Lockers (Men and Women)	135	2	270

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<u>Sketch No.</u>	<u>Room</u>	<u>NSF</u>	<u>Qty.</u>	<u>Extension</u>
29	Cage Washing Room Cage Washer Pass-through autoclave Rinsing Area Rack Holding Area Bottle filler J. Hopper Hooded Dump Station	575	1	575
--	Food and Bedding Storage	80	1	80
--	Trash Holding Room	80	1	80
--	Rack and Cage Storage	200	1	200
--	Procedure Room 1 Laminar Flow hood	165	1	165
--	Immunosuppressed Animals Room Suites (BL-3 potential) 1- cage room at 150 NSF 1- Anteroom at 80 NSF Sink and Counter Double-door pass-through autoclave	230	2	460
--	Small Animal Surgical Suite O.R.	115	1	115
	Prep/Recovery Room	115	1	115
	Instrument Storage	60	1	60
--	Inhalation Facility Control Room (adjacent to 2 cage rooms) 2- 2' x 4' chambers	120	1	120
Subtotal				4,505 NSF
<b>BUILDING SUPPORT</b>				
22	Large Conference Room 12 seats	382	1	382

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<u>Sketch No.</u>	<u>Room</u>	<u>NSF</u>	<u>Qty.</u>	<u>Extension</u>
23	Lecture Room 30 seats	600	1	600
--	Catering Pantry	100	1	100
5	Receiving Office (3 bay loading dock)	116	1	116
--	Vending Area and Break Room	180	1	180
--	Waste Chemical Holding 4' chemical fume hoods	142	1	142
--	Isotope Holding	80	1	80
--	Chemical Receiving, Storage and Dispensing	200	1	200
--	Tank Holding	80	1	80
--	Mail Room	120	1	120
24	Central Glasswashing 1 large autoclave 2 medium autoclaves 1 glasswasher 1 glassdryer Double sink Sorting table	370	1	370
--	Small Office	80	1	80
--	Storage for Glasswashing	80	1	80
--	Building Manager's Office files 2 desks	200	1	200
--	General Storage	800	1	800
--	Graphic Arts Facility Next to Darkroom on one floor	200	1	200
Subtotal				3,730 NSF
Total				32,245 NSF
Net to Gross				1.65
Total				53,204 GSF

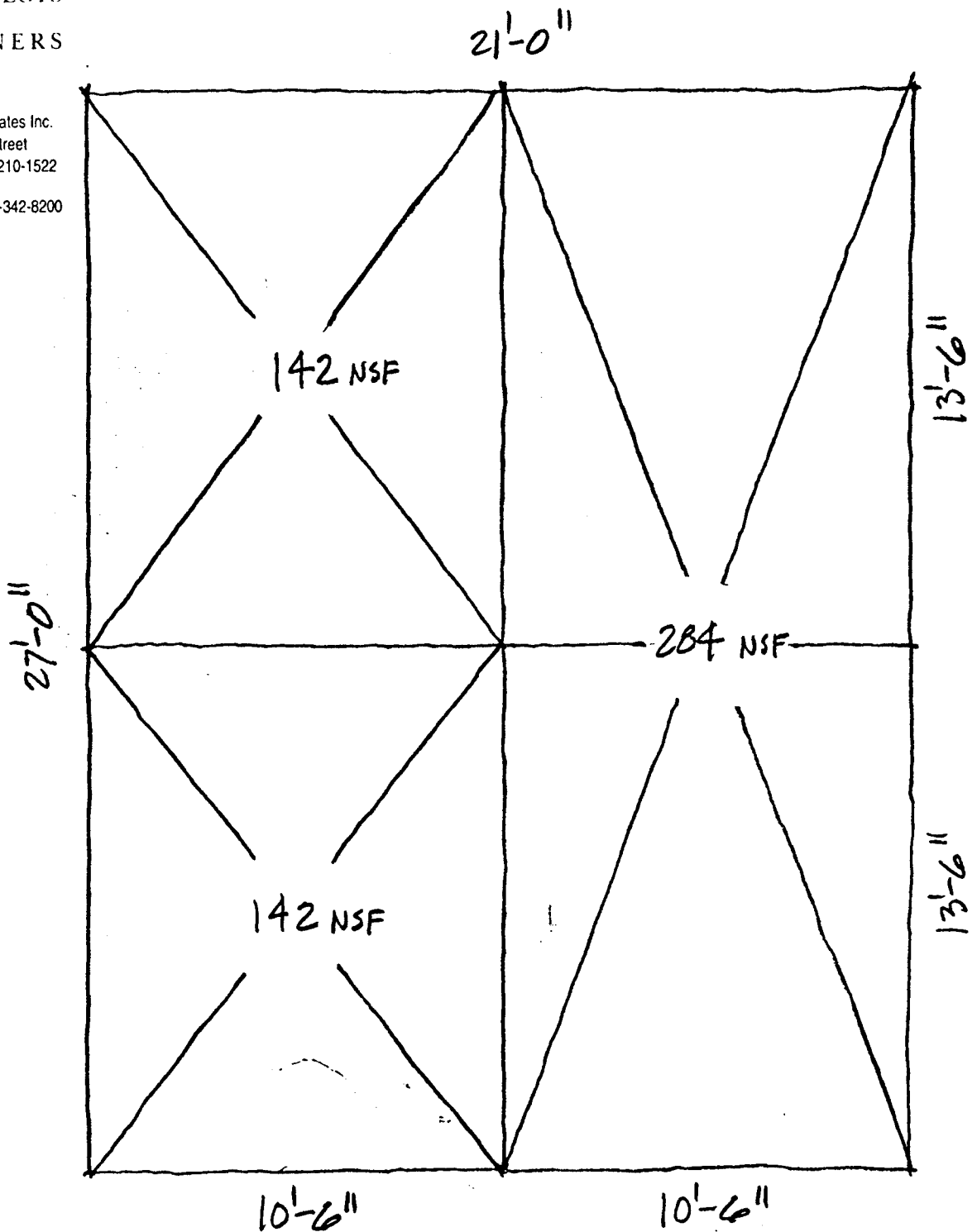
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6. TYPICAL ROOM DIAGRAMS

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1 - SCHEMATIC MODULE

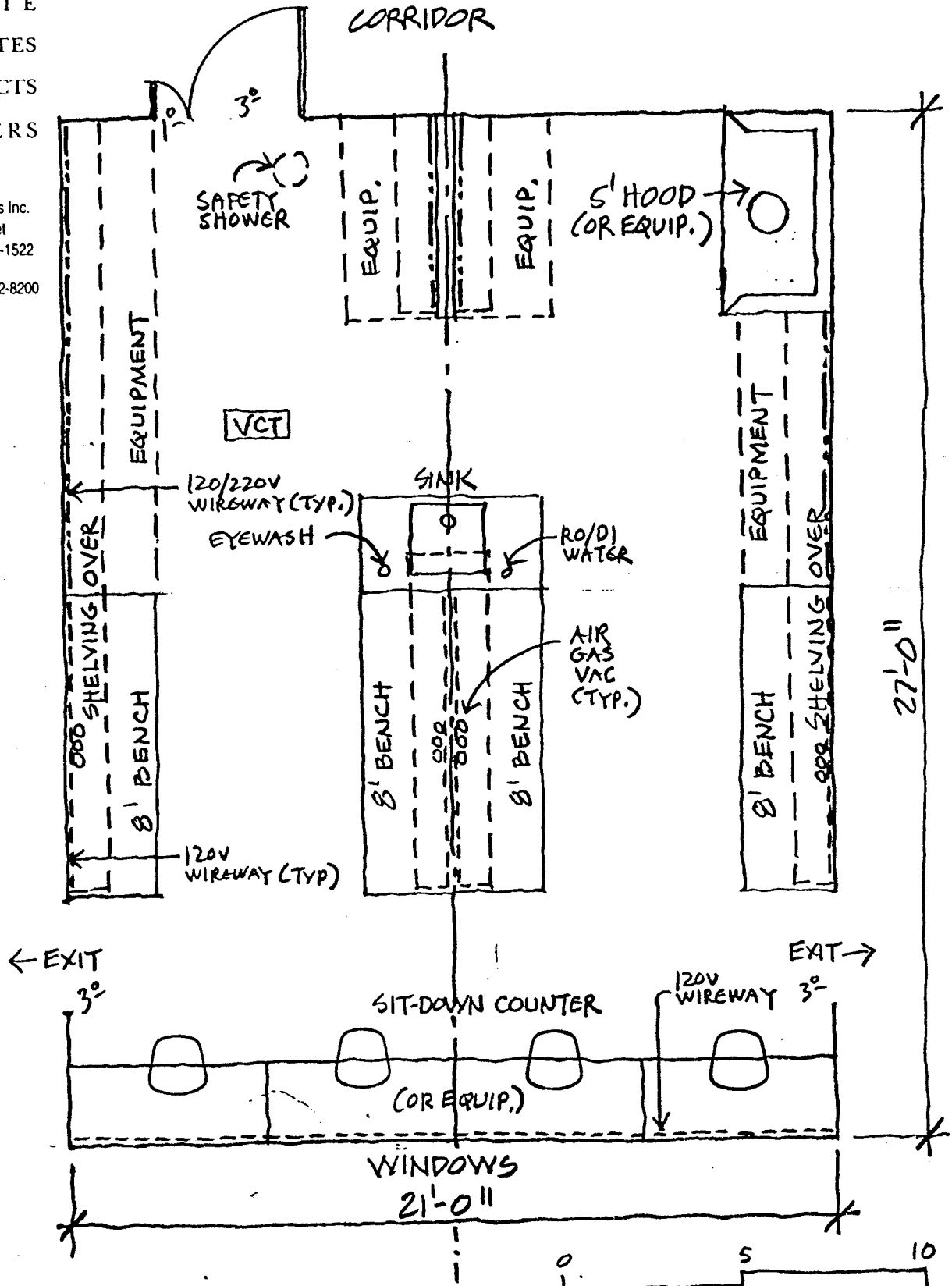




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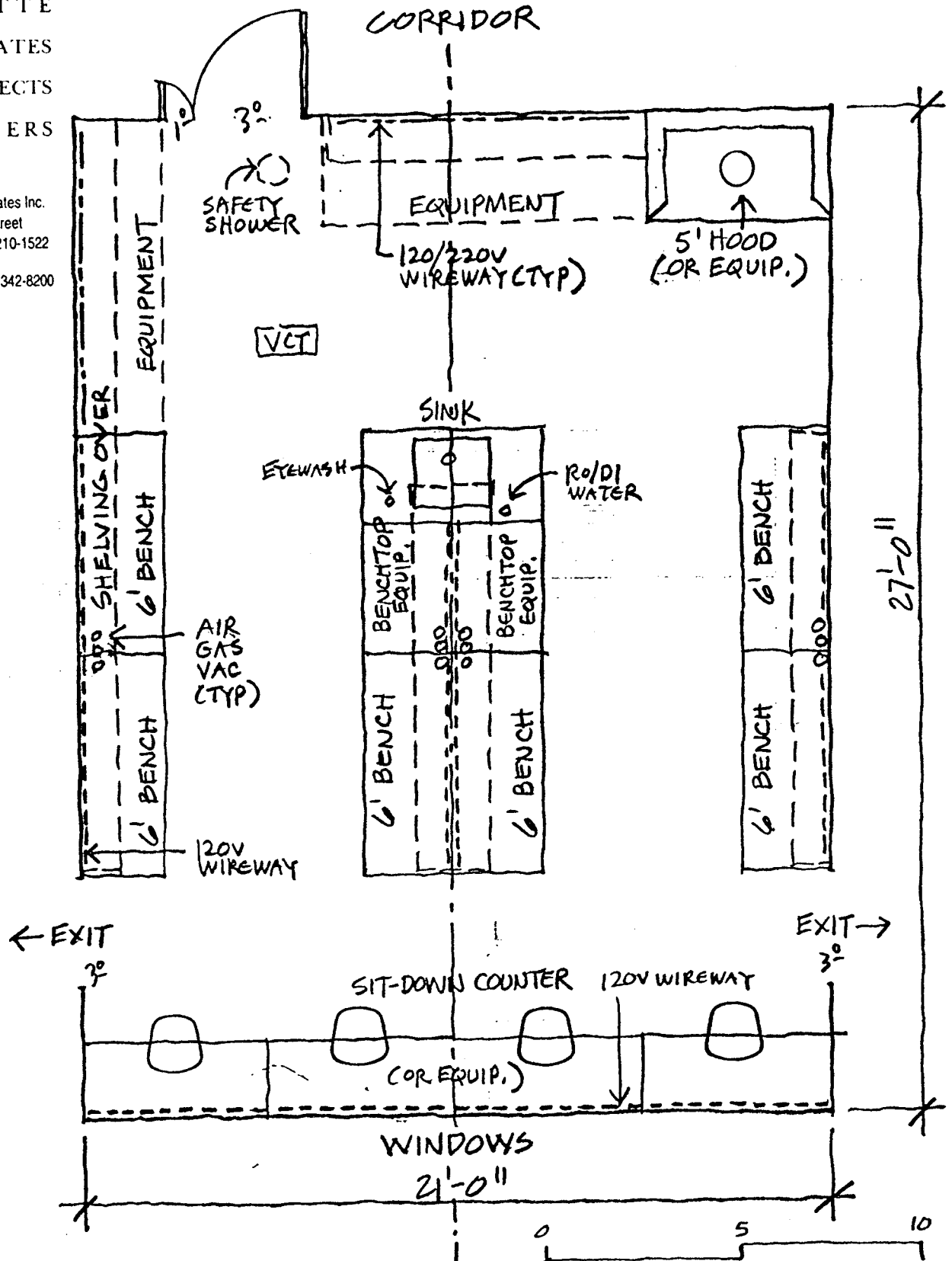
2 - MODULAR LAB - 4 PERSON LAYOUT

21.0' x 27.0' = 567 ASF

29 L.F.E. EQUIPMENT  
32 L.F.E. BENCH

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### 3-MODULAR LAB-6 PERSON LAYOUT

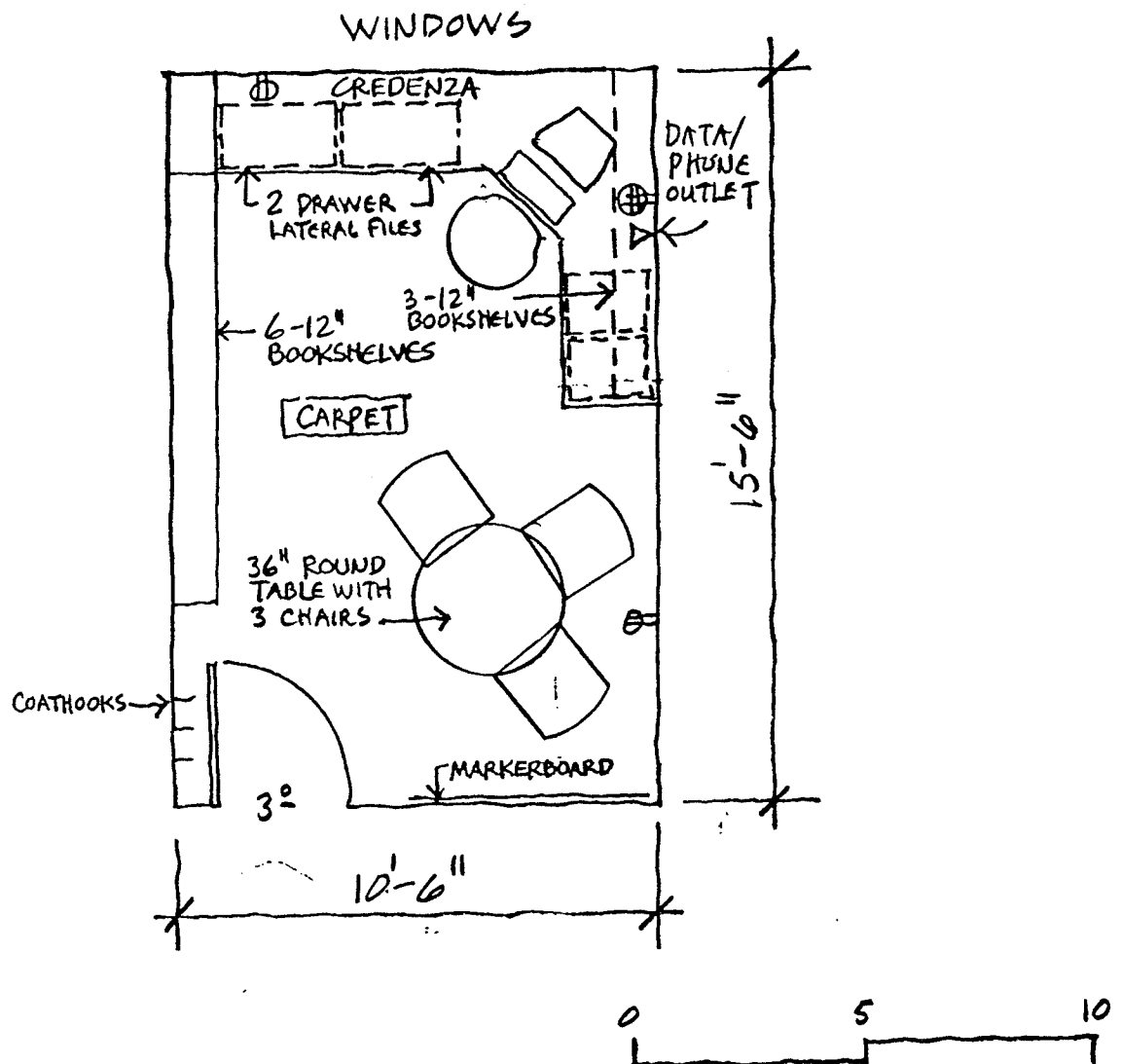
21.0' x 27.0' = 567 ASF

25 L.F.E. EQUIPMENT  
36 L.F.E. BENCH

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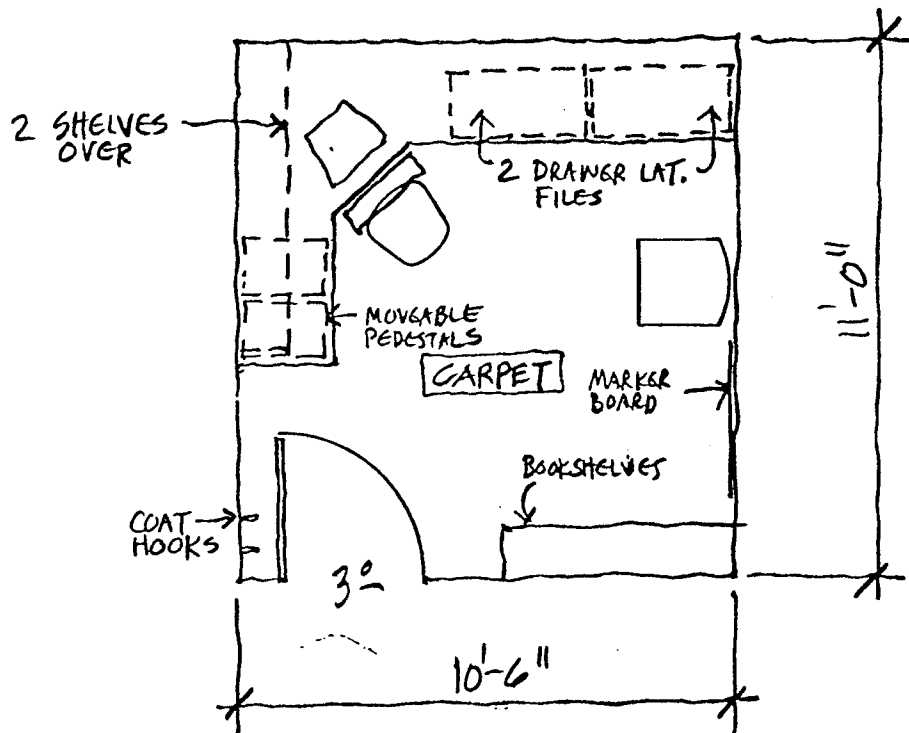
4 - PRINCIPAL INVESTIGATOR OFFICE

10,5' x 15,5' = 165 ASF

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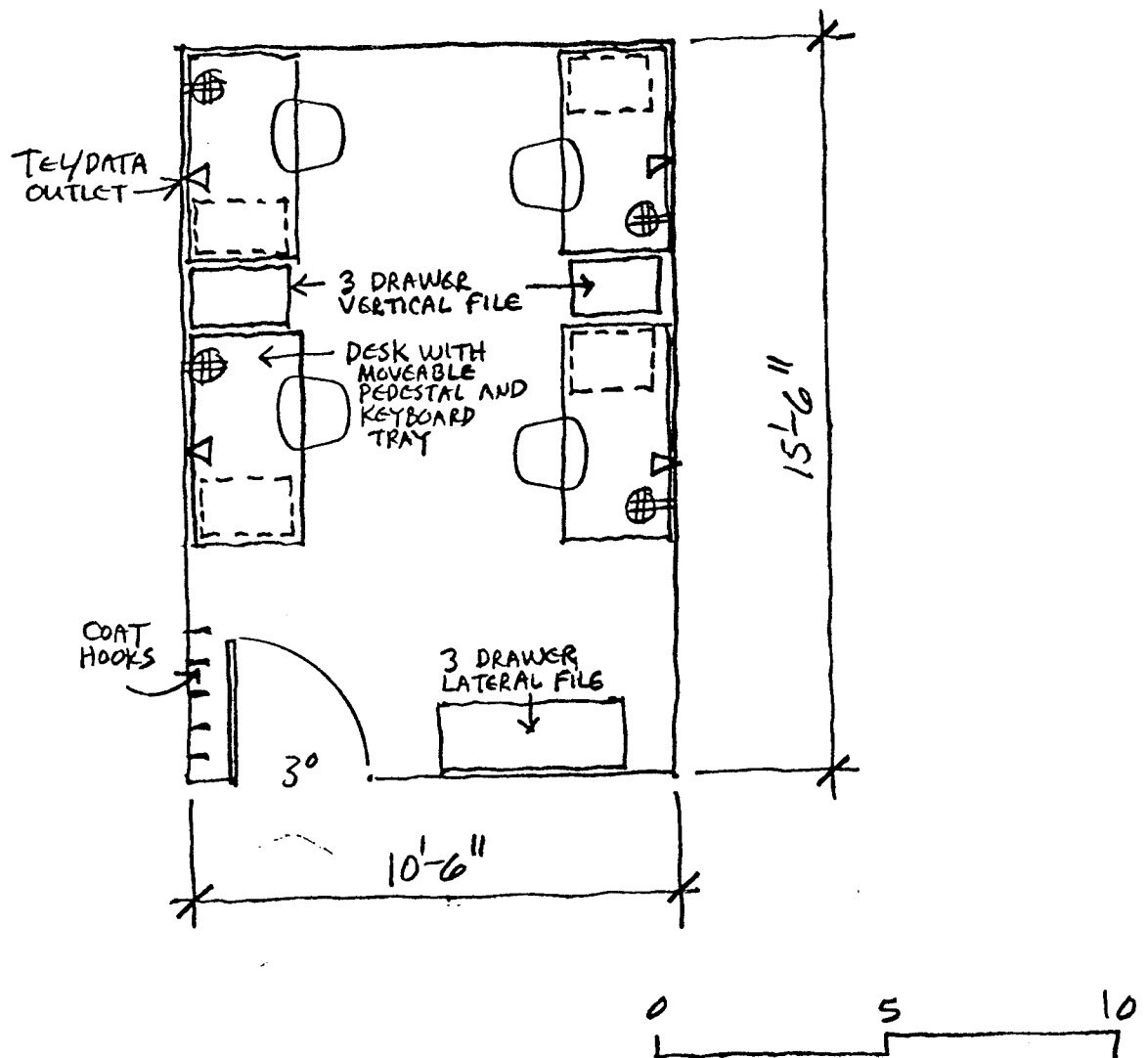
5 - OFFICE

$$10.5' \times 11.0' = 116 \text{ ASF}$$

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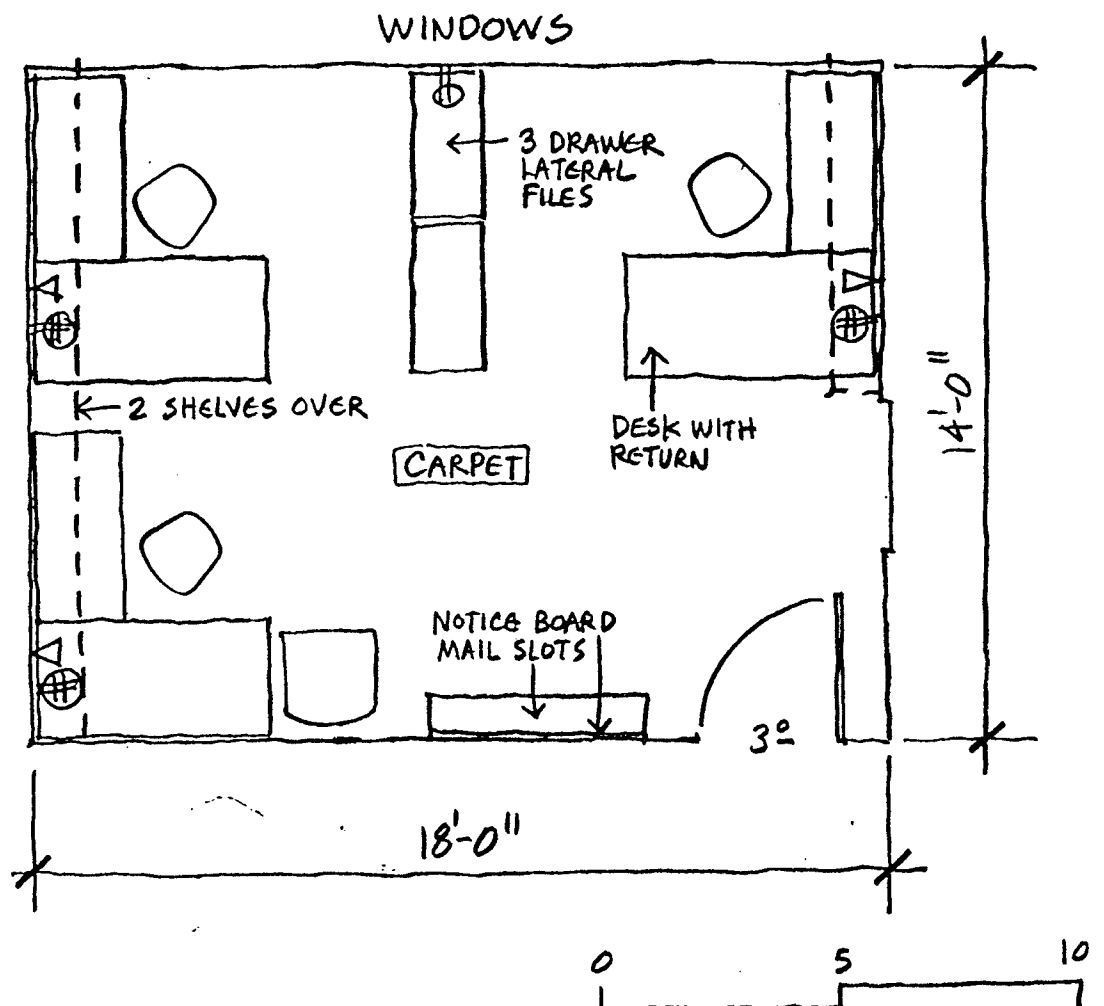


6 - GROUP OFFICE  
10.5' x 15.5' = 165 ASF

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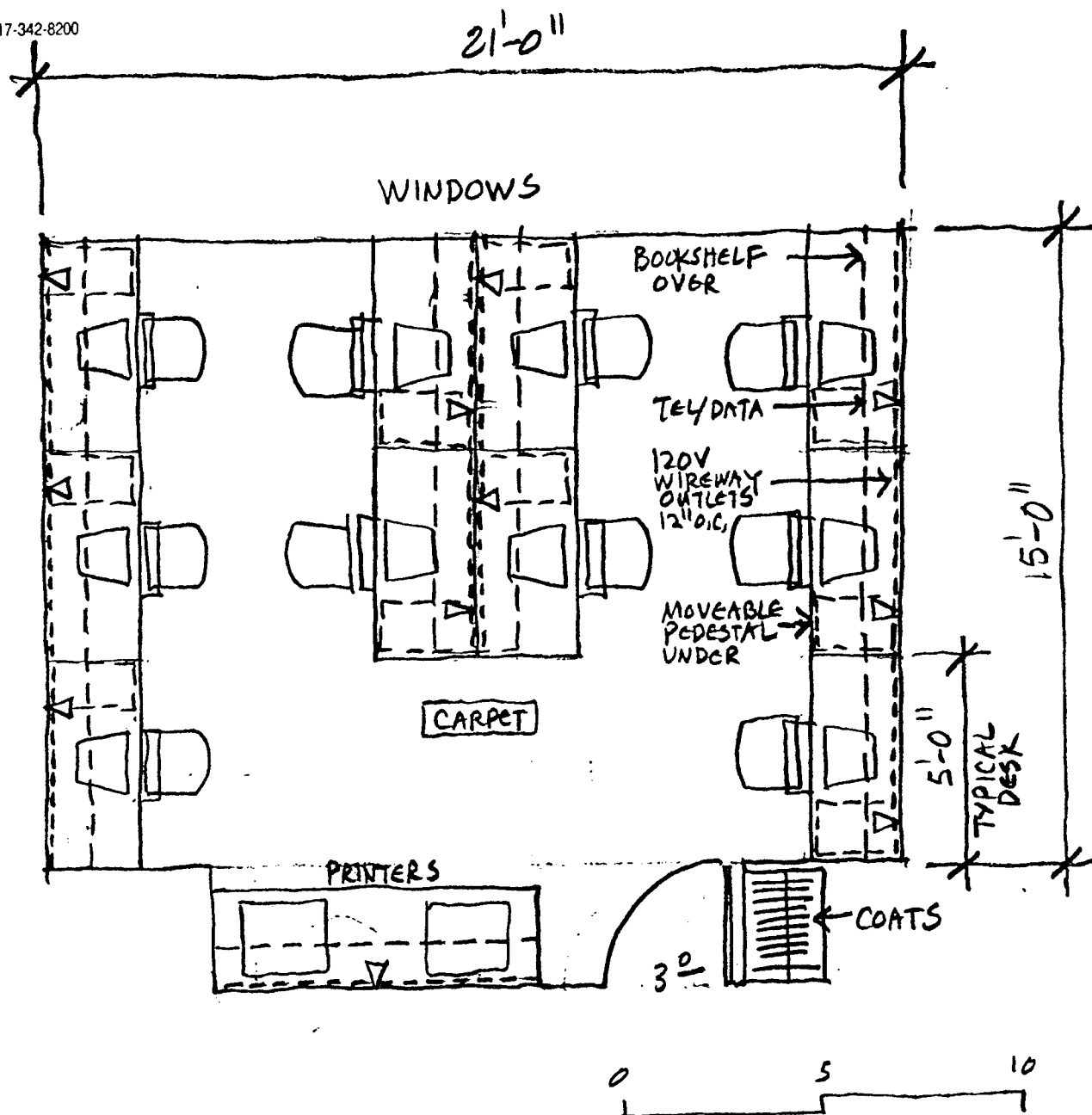


7- SUPPORT OFFICE  
14.0' x 18.0' = 250 ASF

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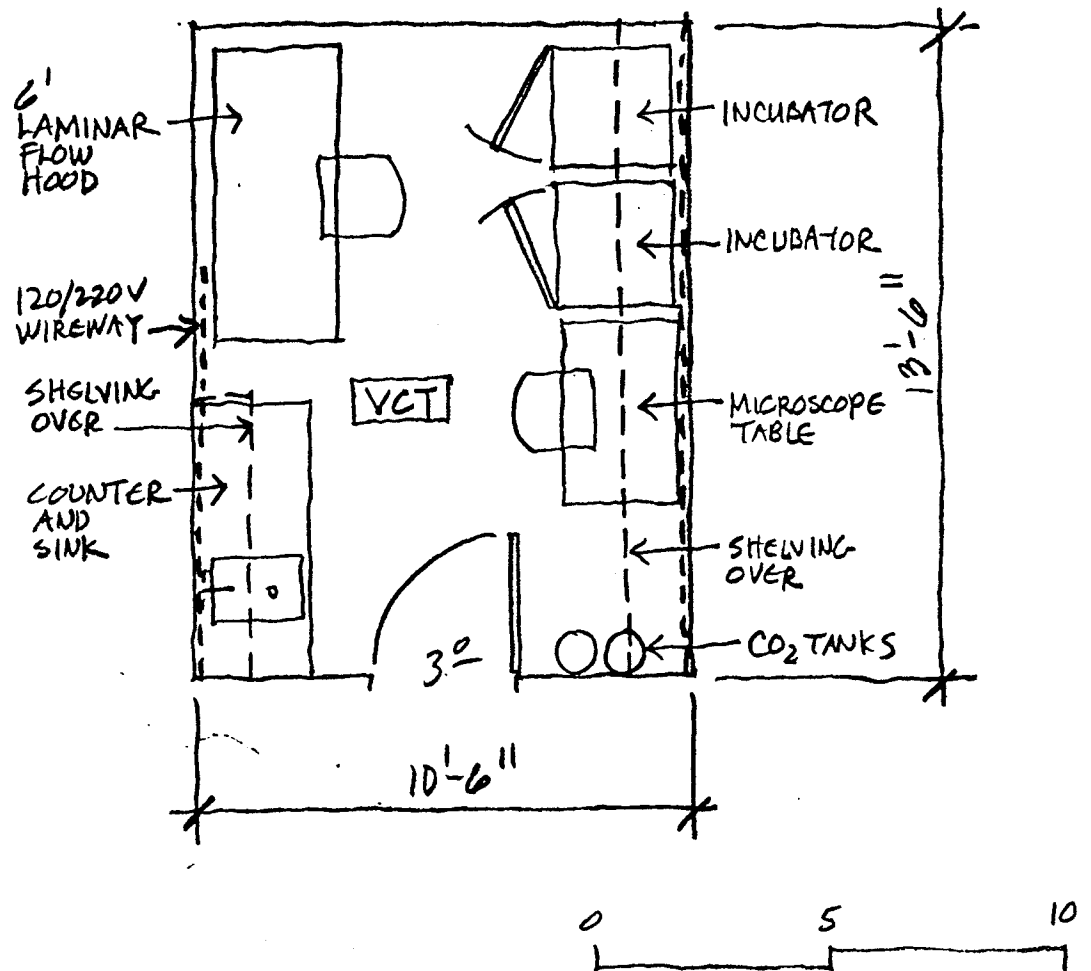


8- STAFF OFFICE  
18.0' x 21.0' = 378 ASF

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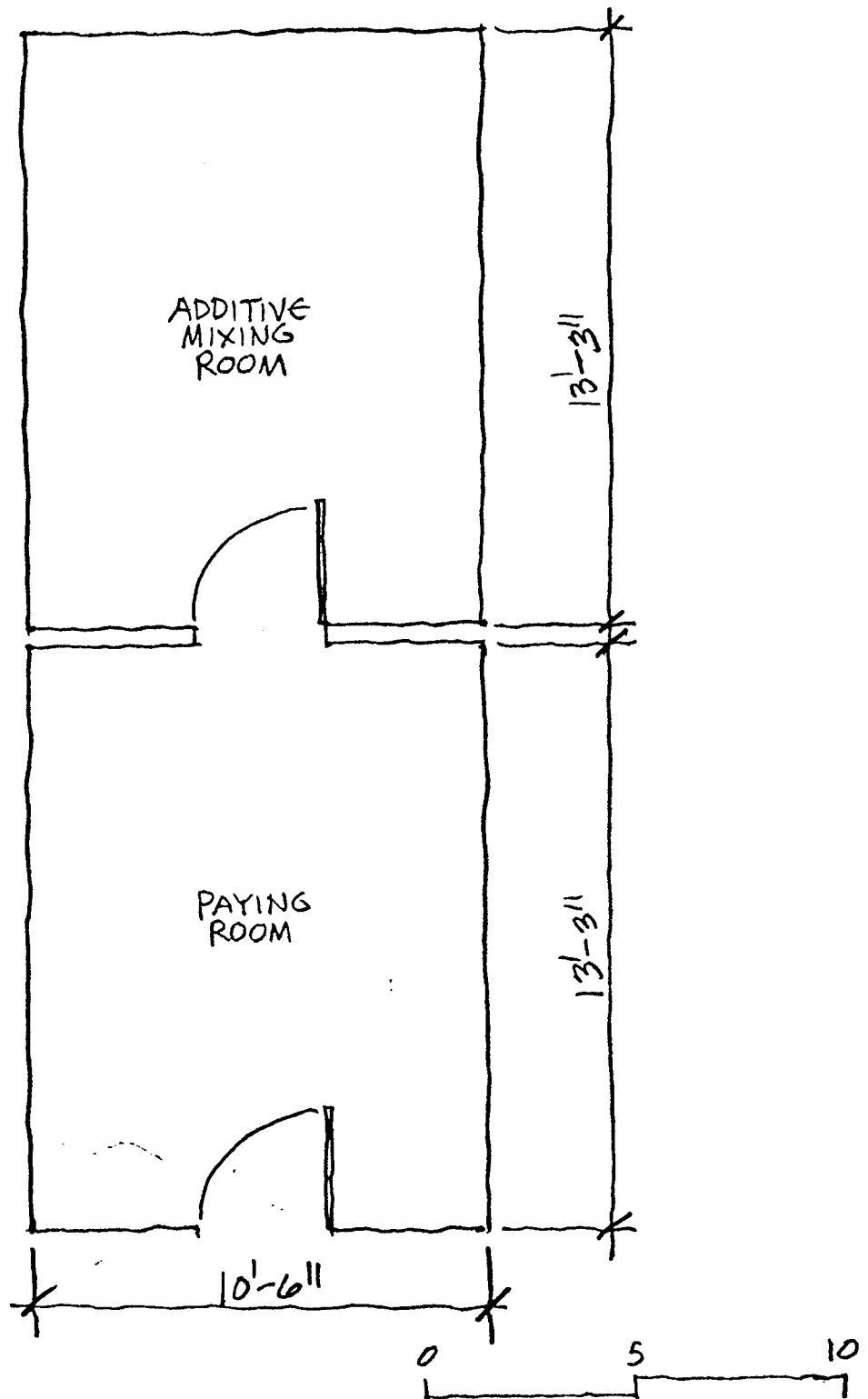
9 - TISSUE CULTURE ROOM  
10.5' x 13.5' = 142 ASF  
(1/4 MODULE)



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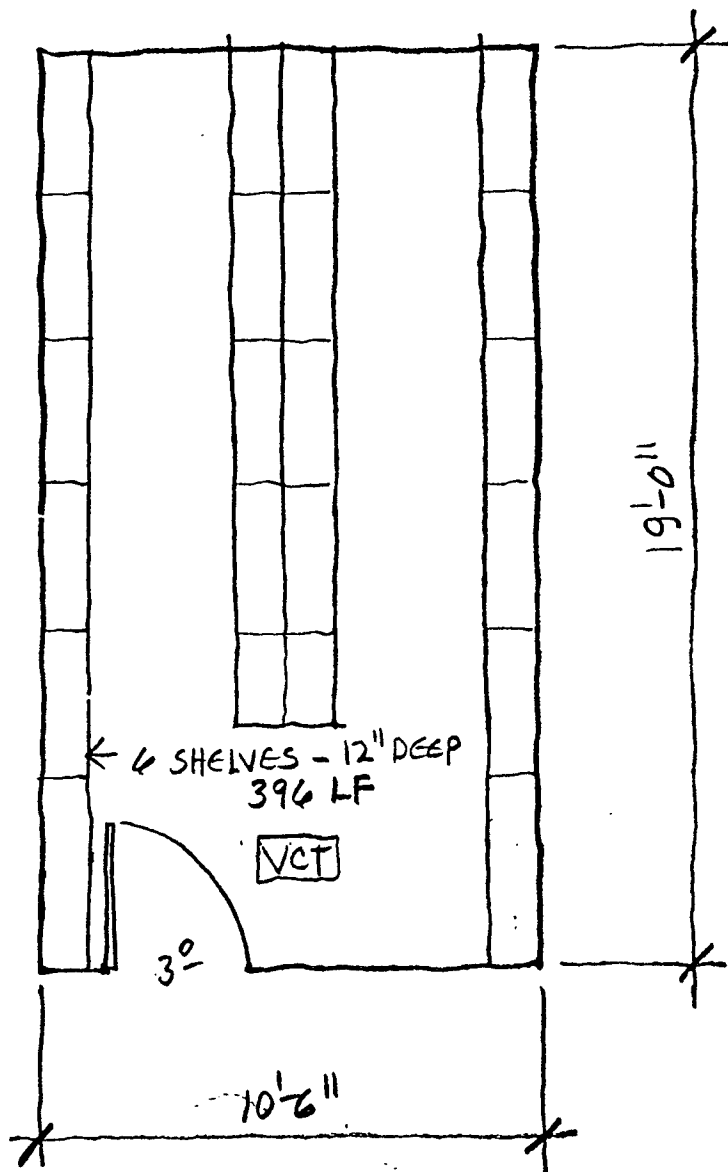


10 - HIGH HAZARD SUITE  
10.5' x 27.0' = 284 ASF

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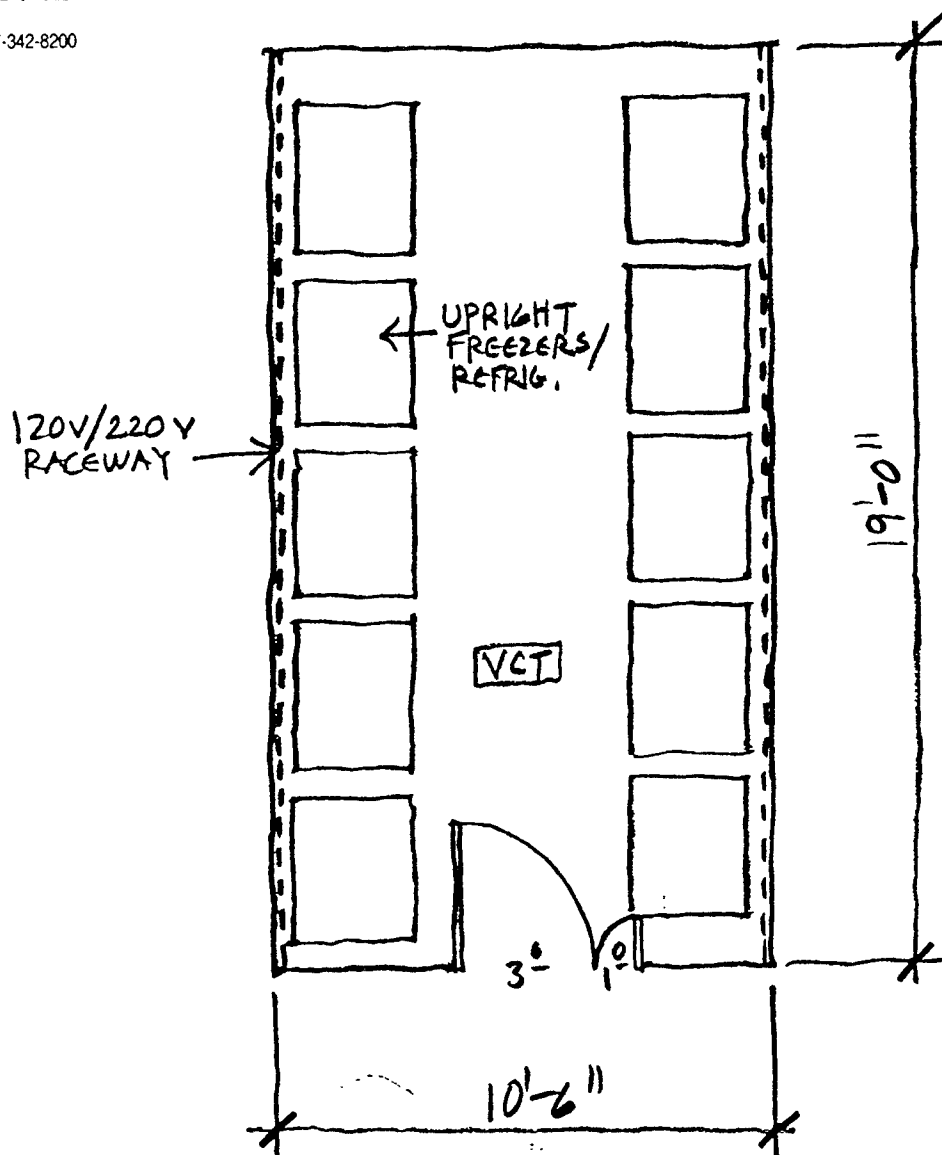


11 - RECORD STORAGE ROOM  
10.5' x 19.0' = 200 ASF

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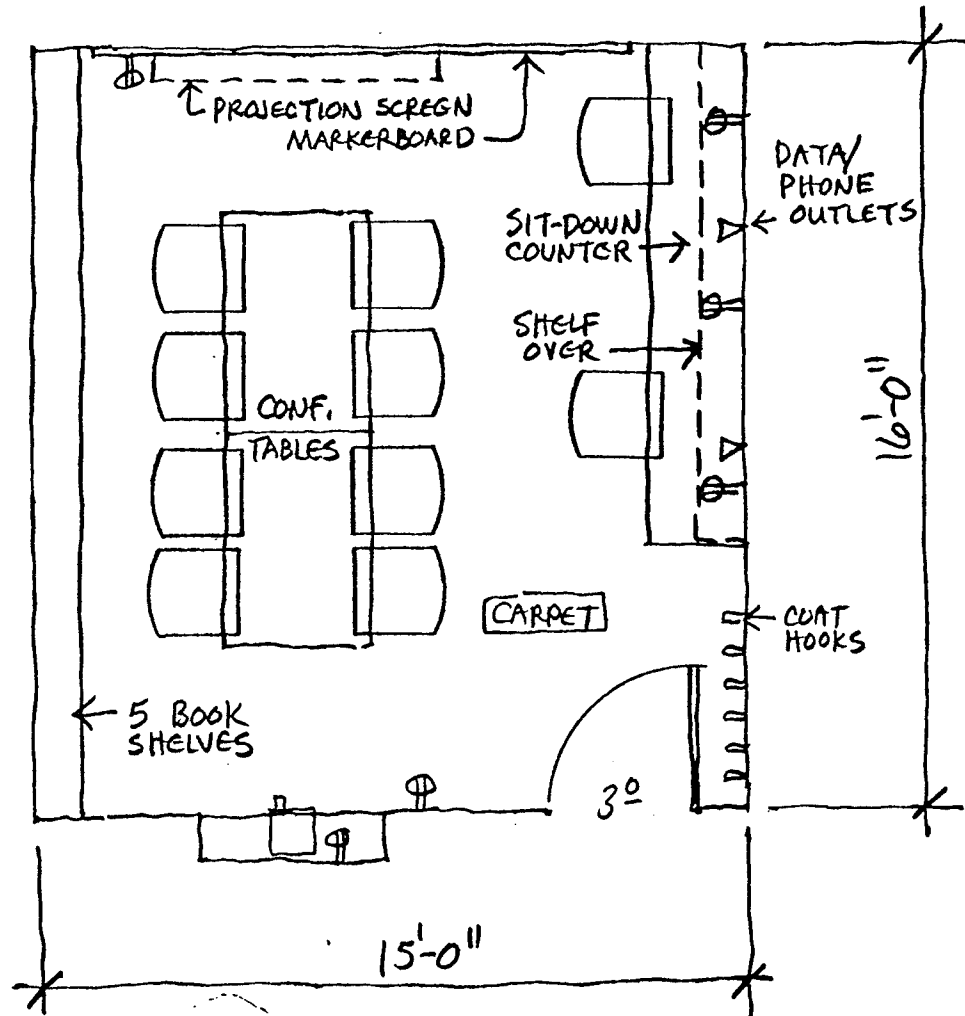


12 - SPECIMEN STORAGE ROOM  
10.5' x 19.0" = 200 ASF

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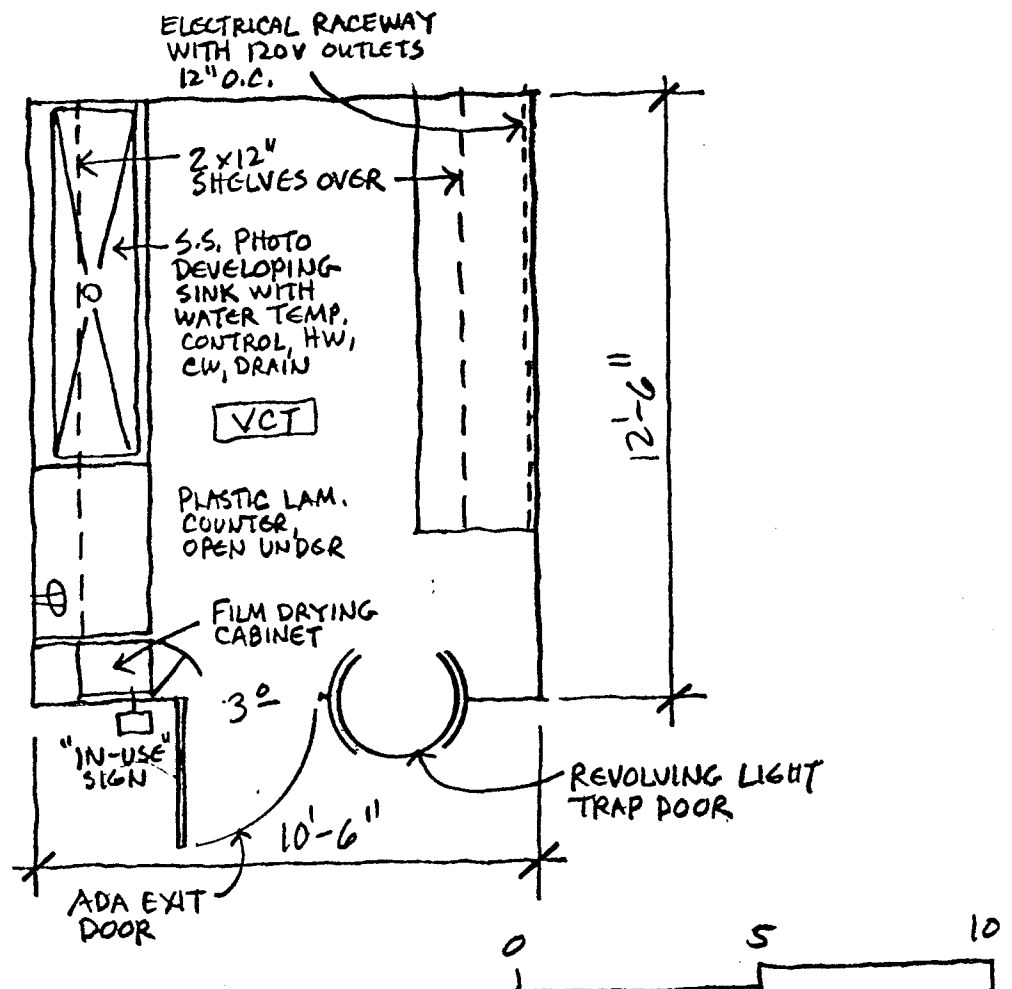


13 - CONFERENCE/LIBRARY  
15.0' x 16.0' = 240 ASF

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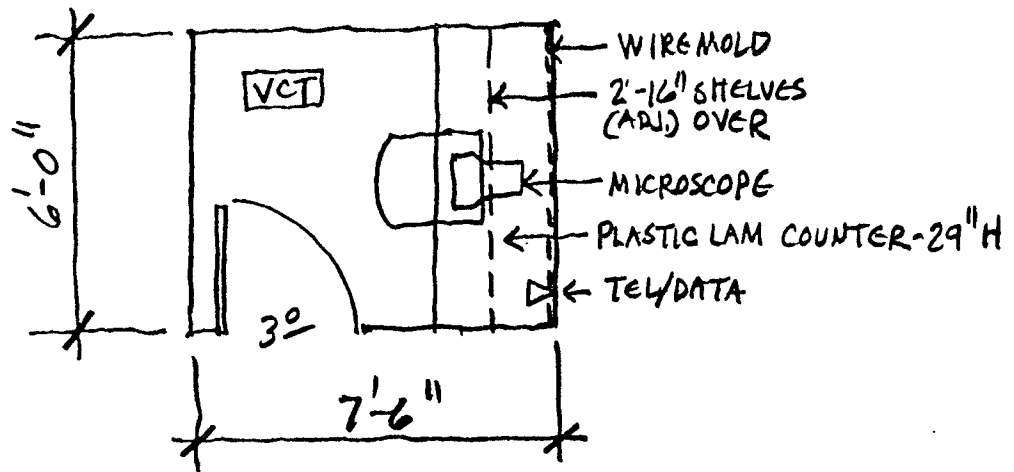
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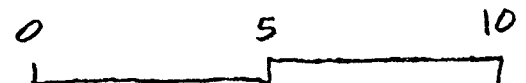
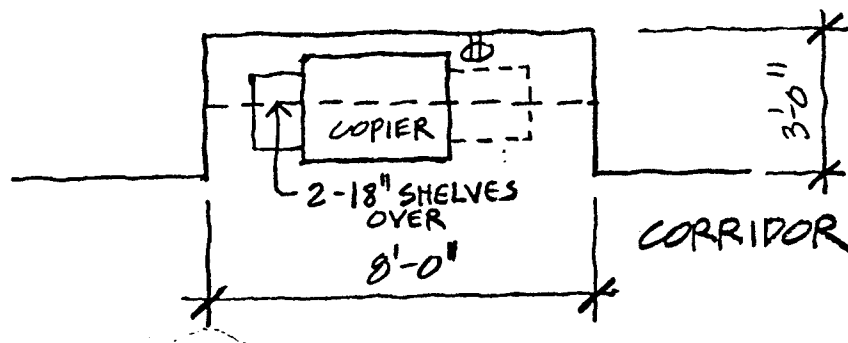
14 - PROCESS DARKROOM  
10.5' x 12.5' = 130 ASF

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16 - FLUORESCENCE MICROSCOPE  
 $6.0' \times 7.5' = 45 \text{ ASF}$

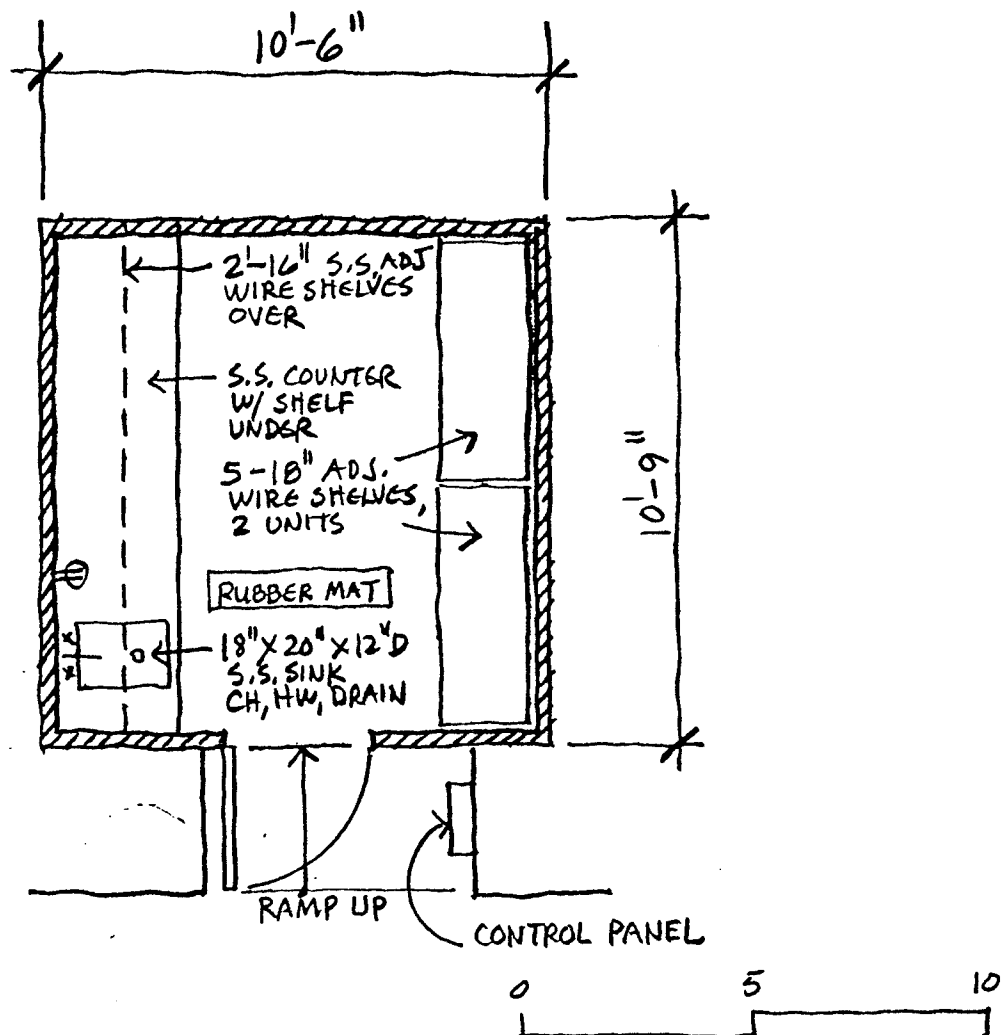


15 - COPIER NOOK  
 $3.0' \times 8.0' = 24 \text{ ASF}$

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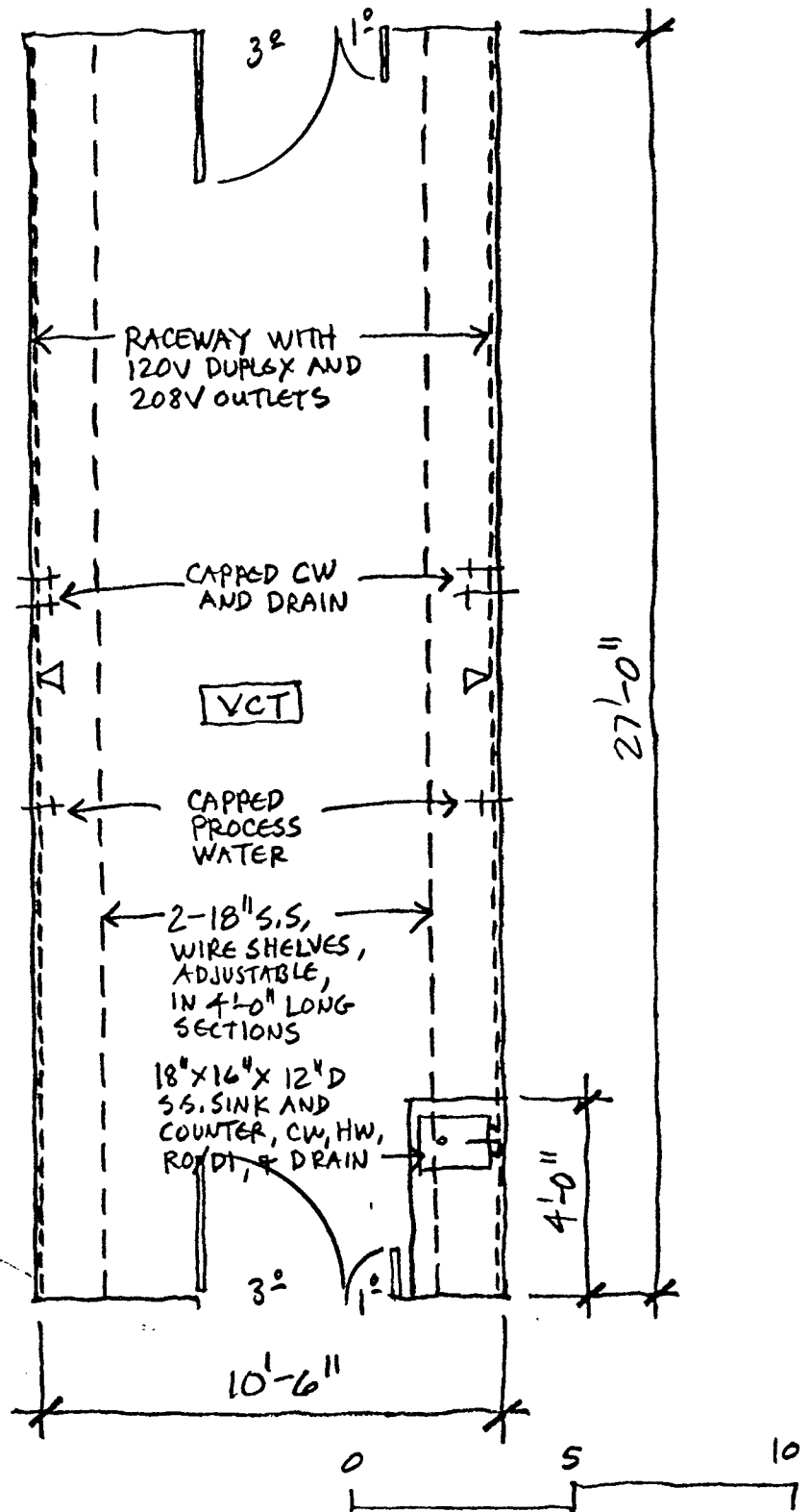


17- COLD ROOM (WARM/COLD ROOM)  
10.5' X 10.75' = 115 ASF

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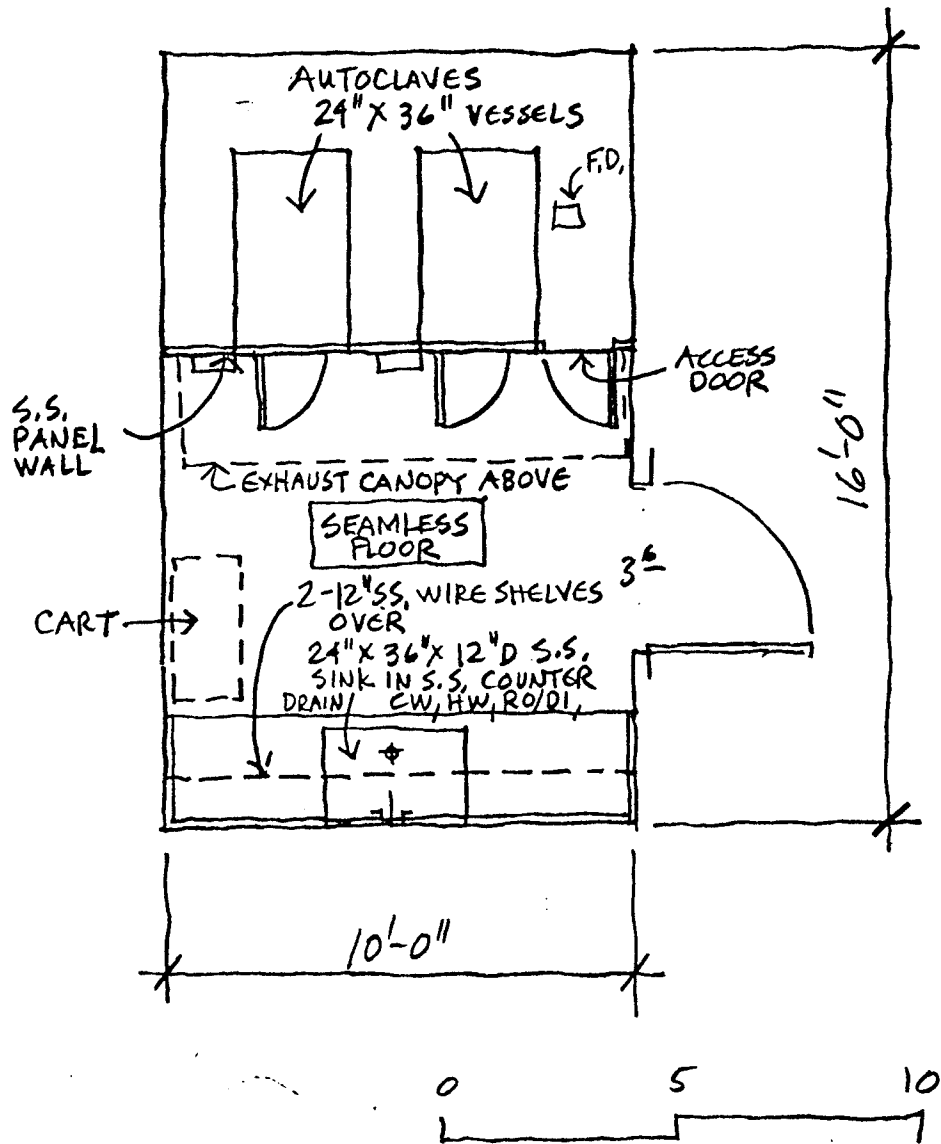


18-EQUIPMENT ROOM  
10.5' x 27.0' = 284 ASF  
(1/2 MODULE)



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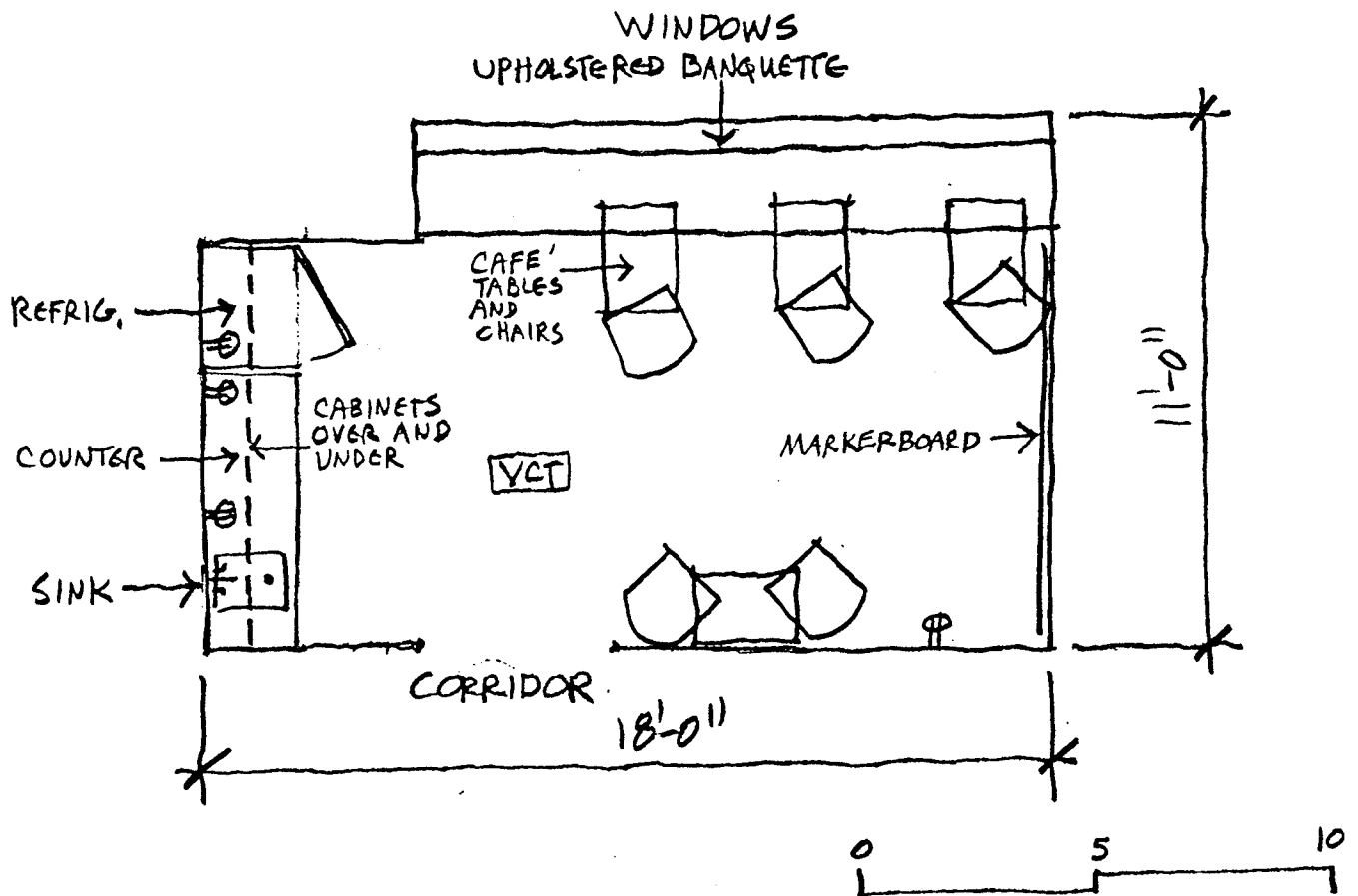


19 - AUTOClave ROOM  
10.0' X 16.0' = 160 ASF

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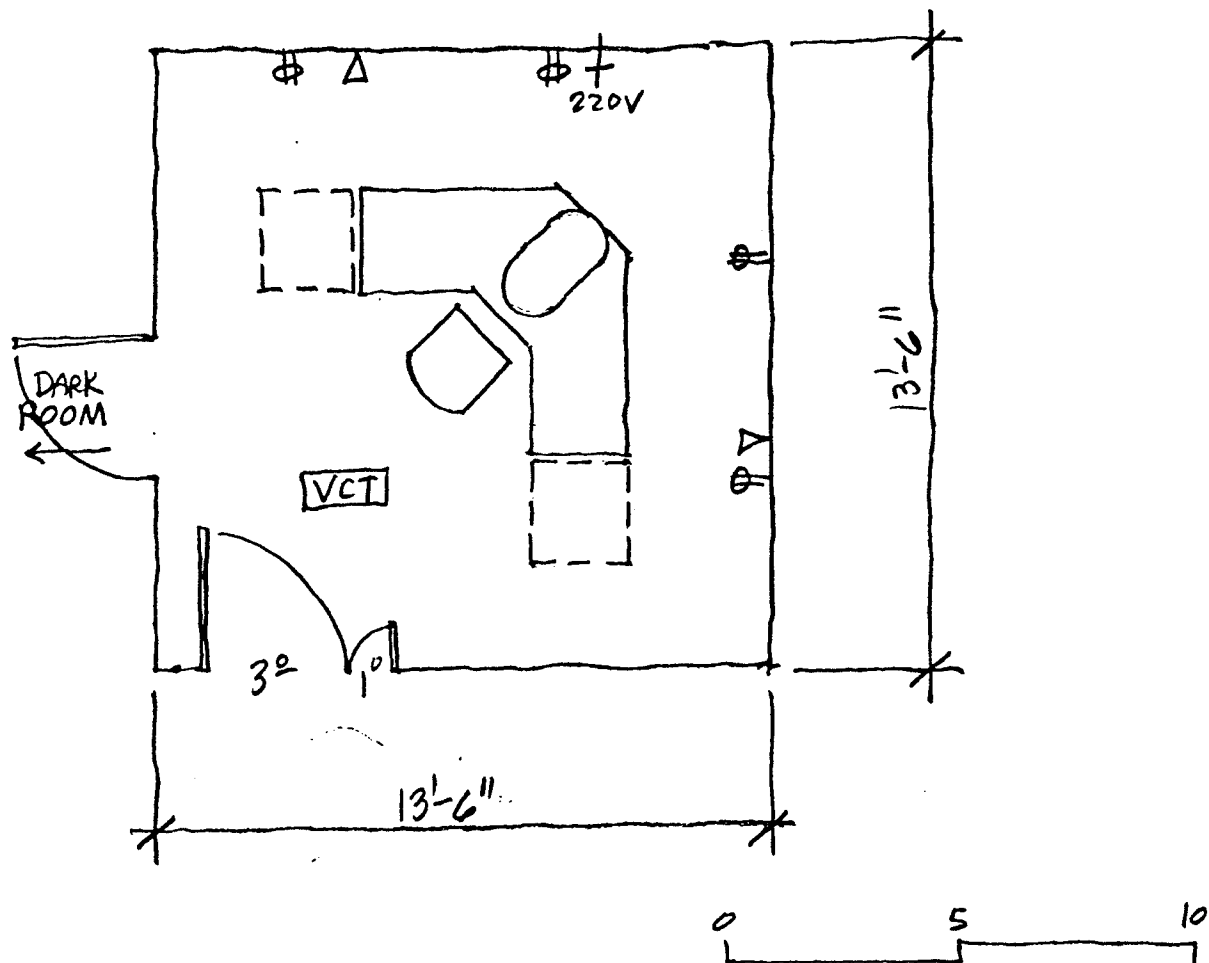


20 - BREAK ROOM + KITCHENETTE  
 $18.0' \times 11.0' = 200 \text{ ASF}$

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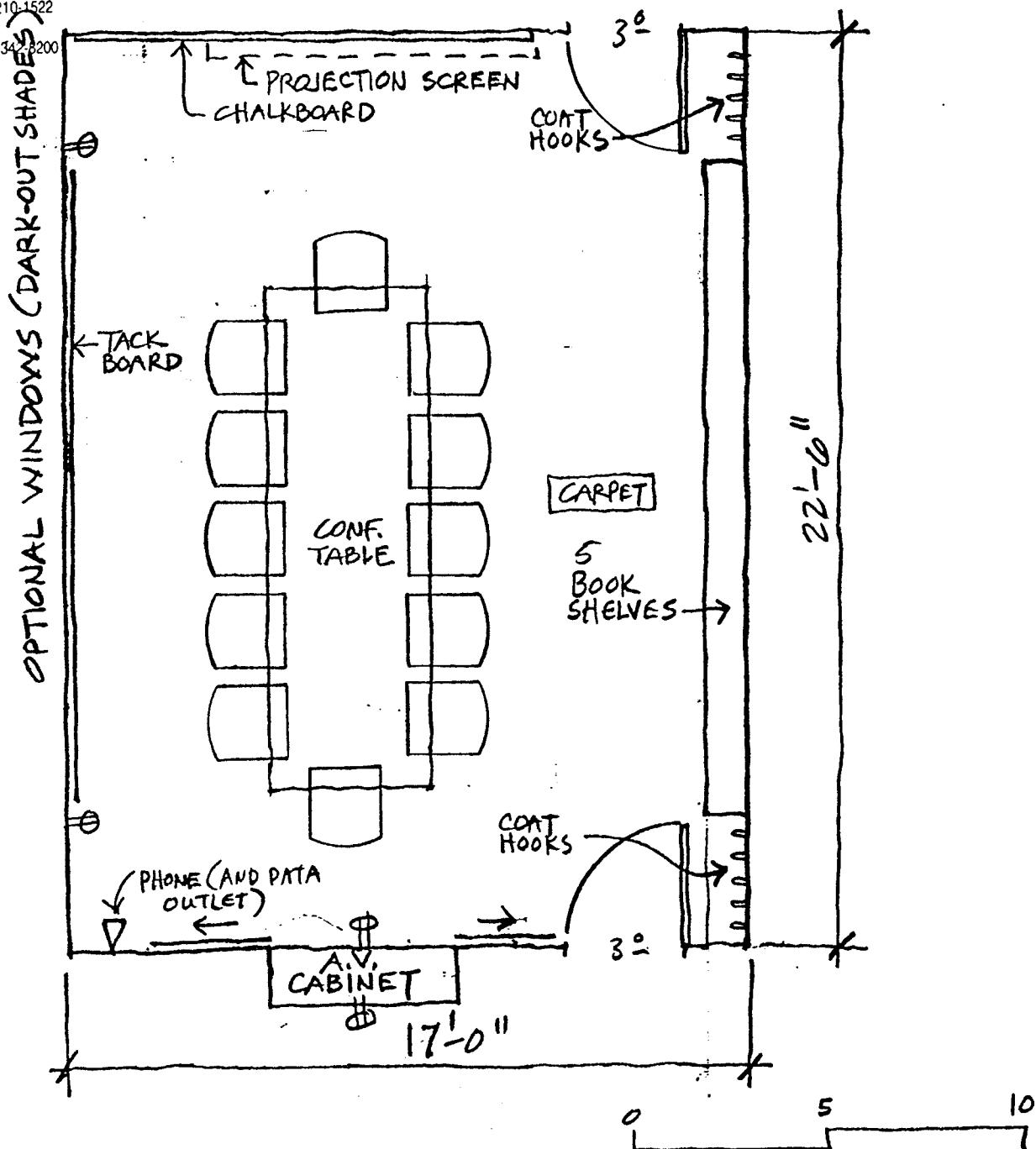


21 - ELECTRON MICROSCOPY ROOM  
13.5' x 13.5' = 180 ASF

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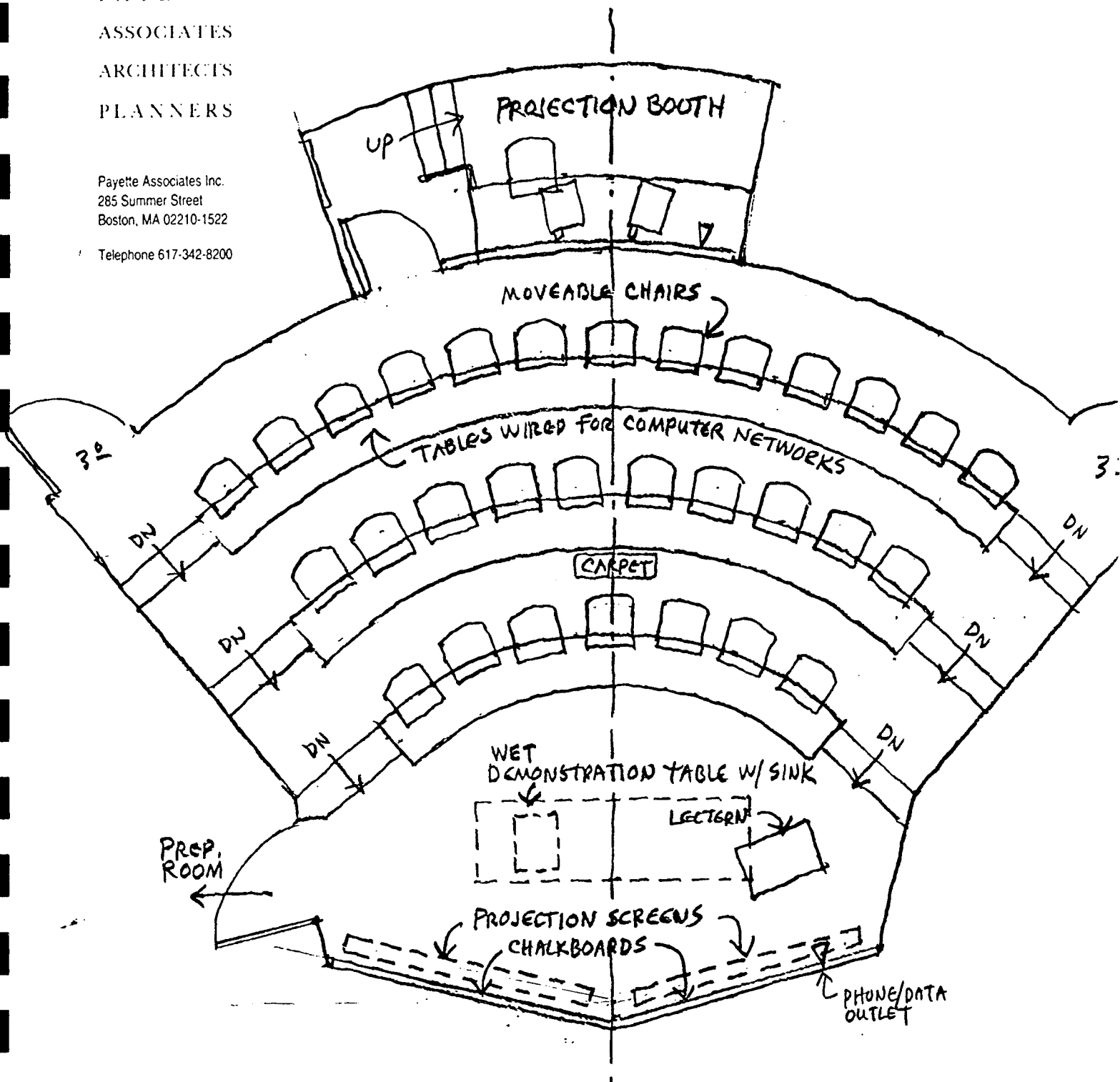


22-LARGE CONFERENCE ROOM  
17.0' x 22.5' = 382 ASF

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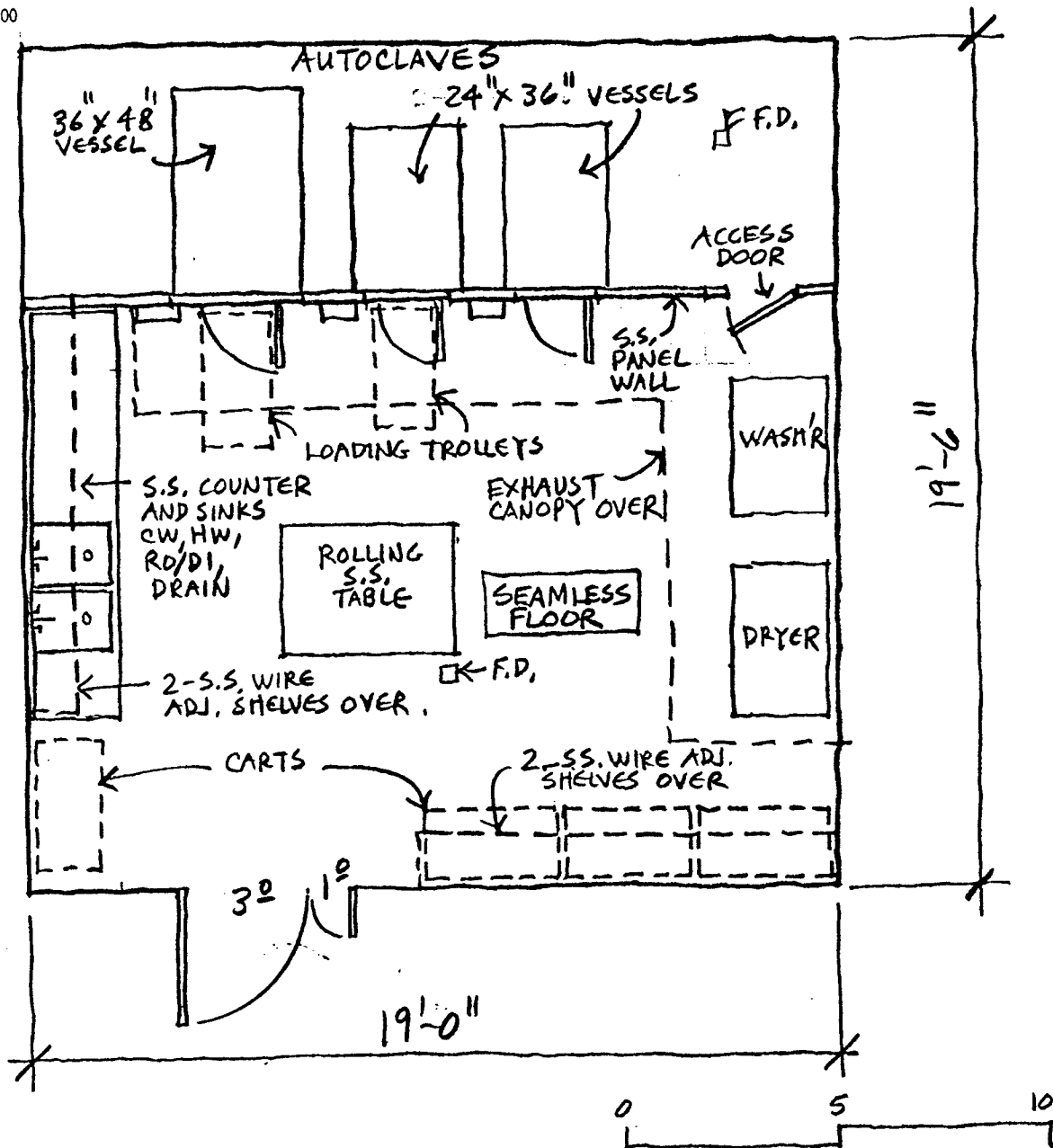
23-LECTURE ROOM  
600 ± ASF

30 SEATS

PAYETTE  
ASSOCIATES  
ARCHITECTS  
PLANNERS

Payette Associates Inc.  
285 Summer Street  
Boston, MA 02210-1522

Telephone 617-342-8200

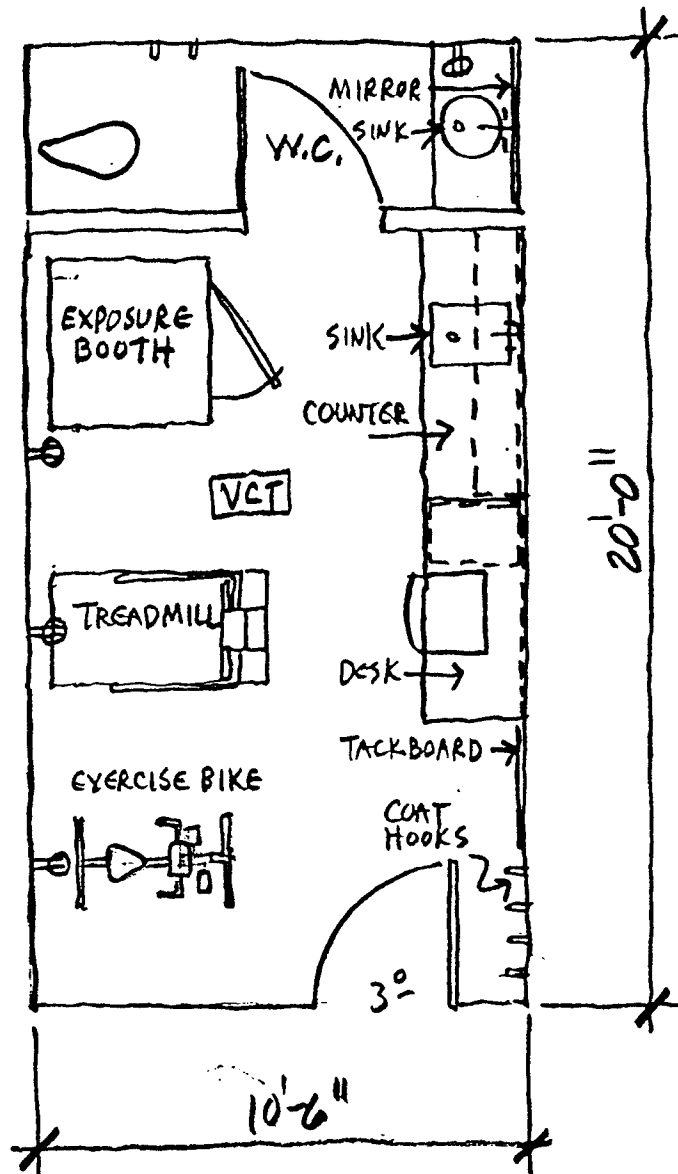


24 - CENTRAL GLASSWASHING  
19.0' x 19.5' = 370 ASF

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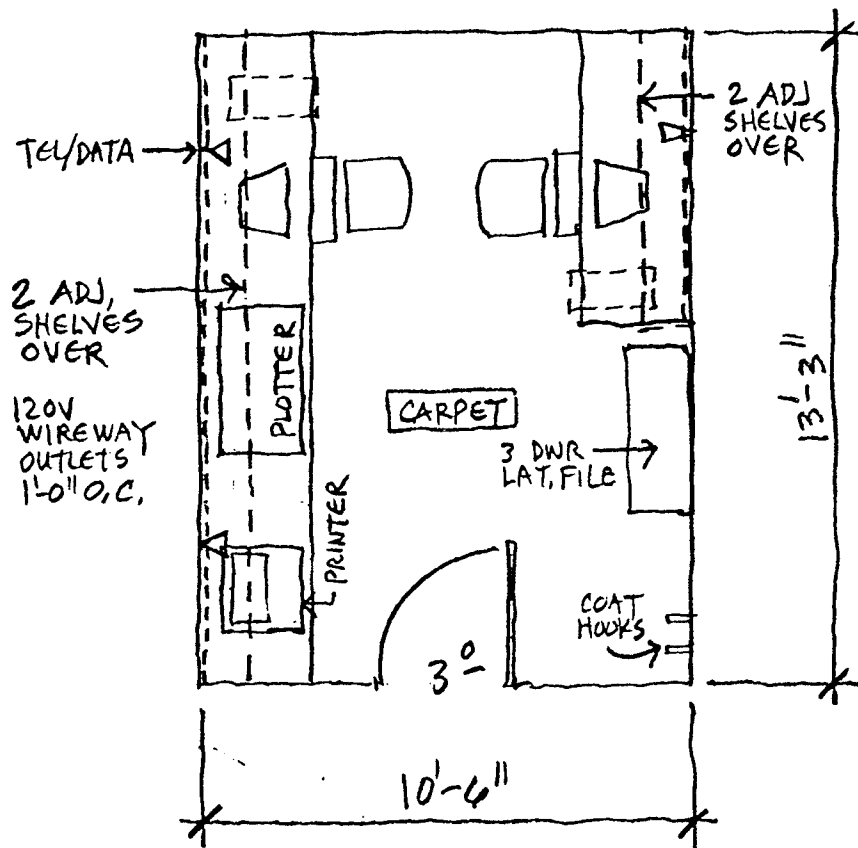


25 - PULMONARY FUNCTION LAB  
10.5' x 20.0' = 210 ASF

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26 - COMPUTATIONAL LAB  
10.5' x 13.25' = 142 ASF

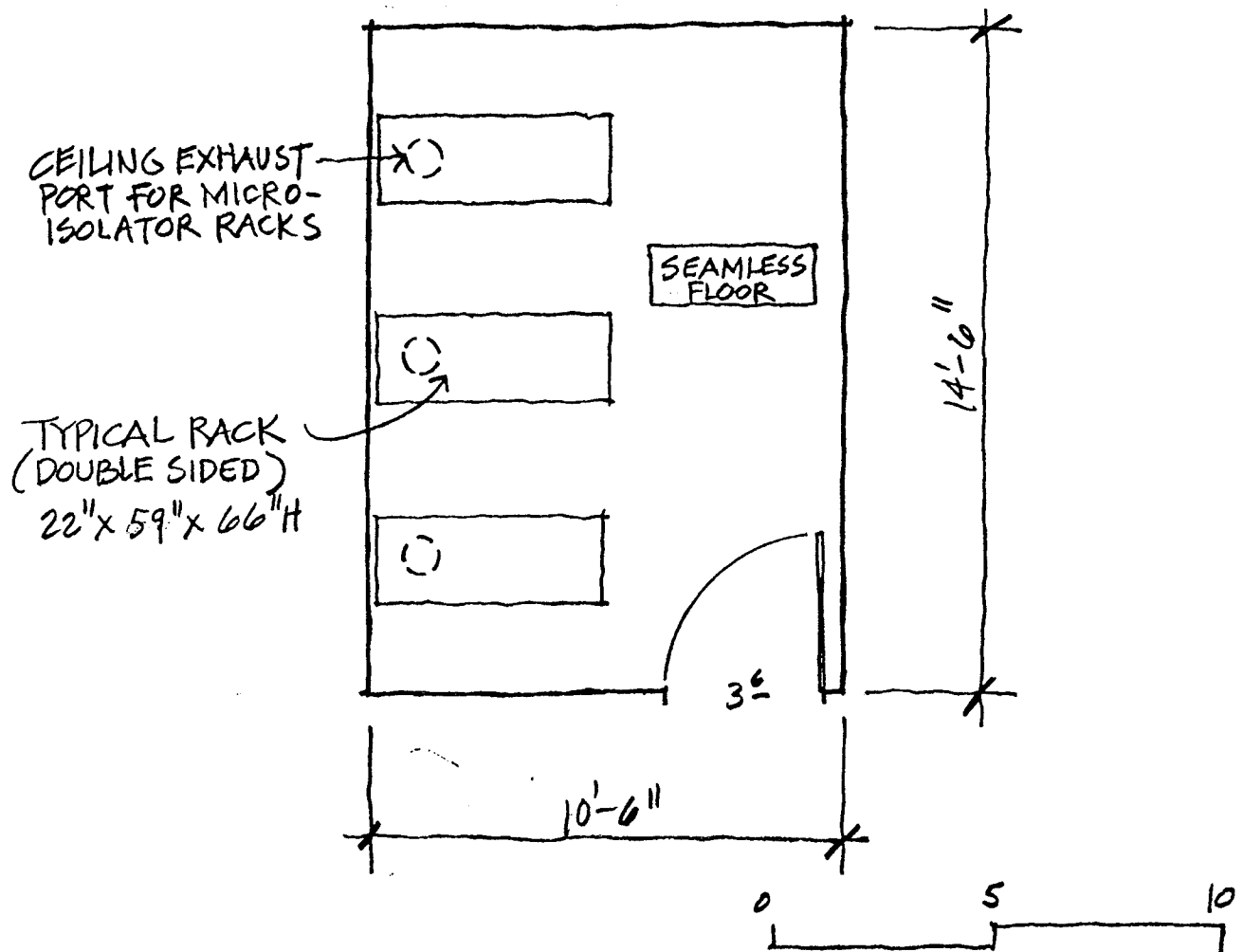
CLOSE TO OFFICES  
CLOSE TO LABS.



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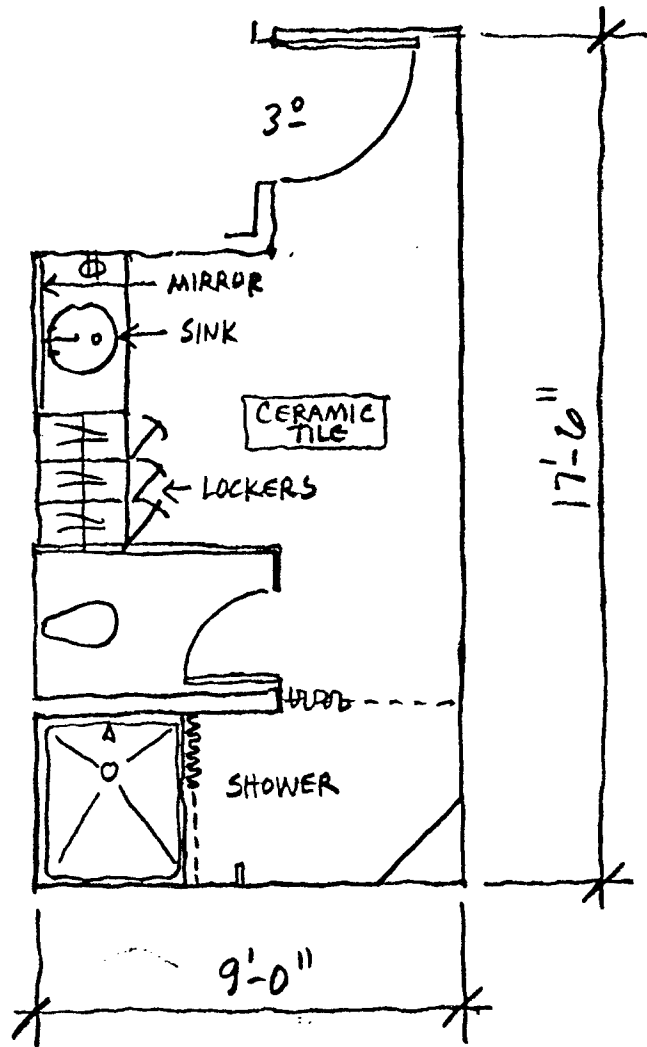
27-TYPICAL ANIMAL CAGE ROOM

$$10.5' \times 14.5' = 150 \text{ ASF}$$

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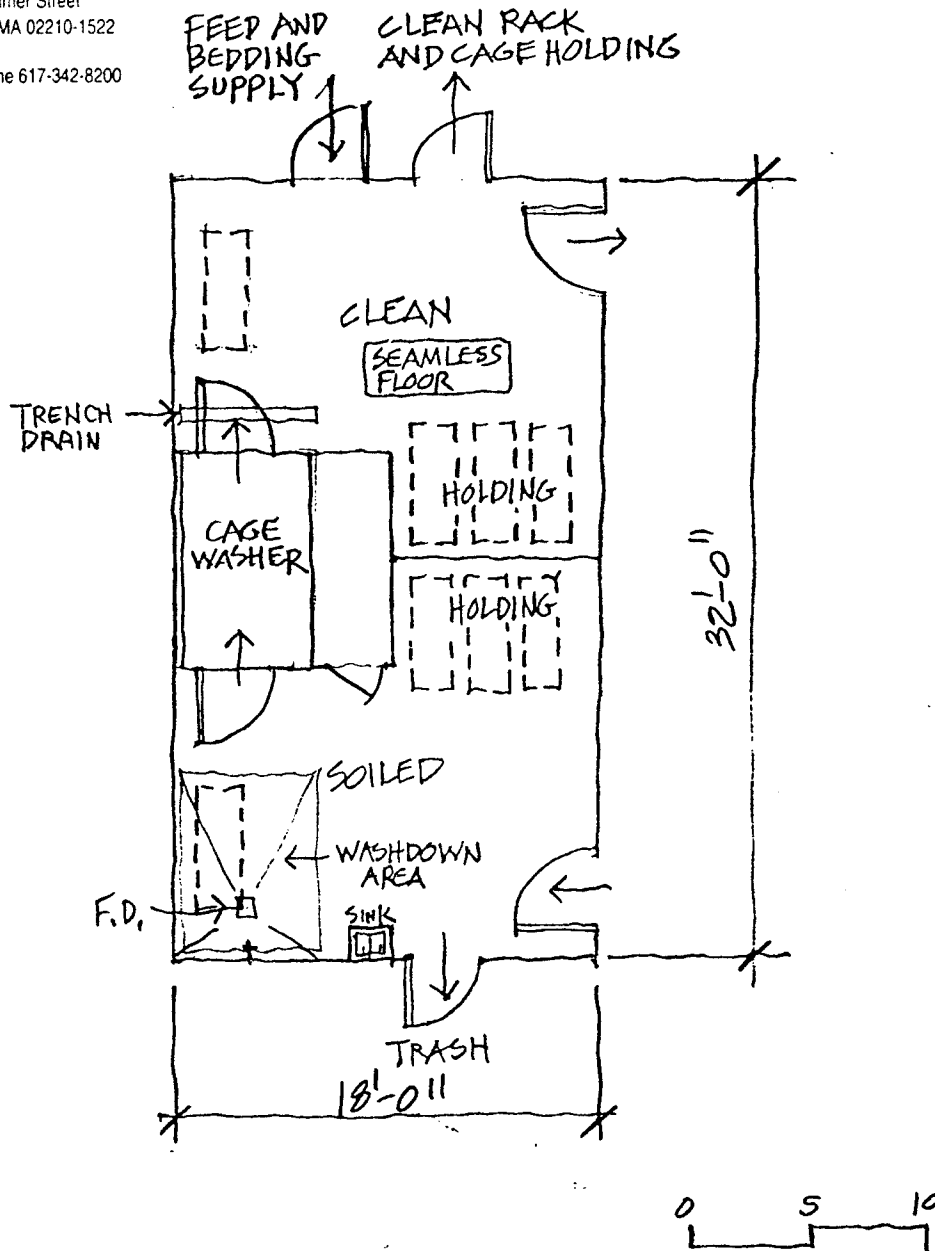


28- RESTROOM/LOCKERS/SHOWER

$9.0' \times 13.0' + = 135 \text{ ASF}$

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ASSOCIATES  
ARCHITECTS  
PLANNERS

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29 - CAGE WASHING ROOM  
 $18.0' \times 32.0' = 575 \text{ ASF}$

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CENTER FOR ENVIRONMENTAL MEDICINE  
PROGRAM DOCUMENT

7. SITE EVALUATION

The site designated for the Center for Environmental Medicine (CEM) is parcel 24 in the Northwest Ohio Advanced Technology Park (NOATP). This site is in the extreme northwest corner of the Park adjacent to Arlington Avenue across the existing railroad line from Parking Lot #4 of the Medical College of Ohio campus (MCO).

The closest existing MCO buildings would be Mulford Library or the Health Science Building. A CEM building on this site would be approximately 1600 feet across parking lot 4, a five minute walk from two buildings with appropriate walkways in place.

Presently most of the MCO buildings are grouped together with large parking lots on the periphery of the campus. Plans are underway to construct a new Nursing and Allied Health Classroom Building to the east of the Health Science Building in the area of the southwest corner of parking lot #4, expanding the MCO complex somewhat in the direction of the NOATP and the proposed CEM site.

One of the functions proposed for the CEM is to spearhead development of the NOATP and create a working linkage between MCO and private industry for technology transfer and communication. Parcel 23, adjacent and to the east of parcel 24, was in fact designated the site of a first biotechnology incubator building. With the above developments, removal of the existing railway line between MCO and NOATP and construction of planned new roadways, parcel 24 will be a pivotal location to link these two campuses.

Interviews with CEM faculty indicate a desire for a convenient walking linkage between the CEM and the Medical College Hospital and the Health Center building for those investigators who also have active clinical practices. No site on the NOATP will be close enough to these two buildings to realistically suggest covered or enclosed walkways. It seems that a desire to walk back and forth under cover may be incompatible with the larger role the CEM can play in linking the two campuses together functionally. On the other hand, a site within the "inner circle" of MCO buildings would not function in the same degree to spearhead development of the technology park.

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Site Evaluation (continued)

Major medical campuses exist in which faculty walk such distances between research areas and patient care areas. Well defined outdoor space, paved walkways, landscaping and level terrain will contribute towards making the walking experience reasonably direct, pleasant and safe; indeed, "campus" like.

The other element of obvious importance is conference and meeting room spaces. Minimal conference facilities have been included in the space program since good meeting rooms already exist in the Dana Center and the Toledo Hilton on Campus. Only one small lecture room of 30 seat capacity has been included. The Dana Center is, however, on the southwest corner of the MCO campus, not a convenient walk from the proposed CEM site. It may not be functionally important for scientific conferences presented by the CEM to take place in the CEM building, but the identity of its role in technology transfer and spearhead to NOATP development may argue for more conference space at the CEM site.

On the other hand, holding major CEM conference activity at the Dana Center will associate CEM research activity with MCO and will make security at CEM easier to achieve.

The development of NOATP roadways, recently approved and funded, will place parcel 24 at a key intersection of Arlington Avenue and the main Tech. Park boulevard route from the city of Toledo and University of Toledo. All necessary utilities will be provided as part of the park development.

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PROGRAM DOCUMENT

8. ENGINEERING SYSTEMS DESCRIPTIONS

HVAC

Supply air to laboratories, 100% outside air no recirculation.

One air handling unit, with multiple fan sections for redundancy, located at basement level or at penthouse level. An all-air constant volume/variable volume type will incorporate axial adjustable pitch variable air volume fans. Variable amounts of air will be delivered to each room in direct proportion to the interior space conditions and/or exhaust requirements via fume hood or room exhaust. Control system to be DDC.

Each laboratory module and each room will have a heat and air-condition zone controlled by its own thermostat. Positive or negative pressure relationships will be established between each room, adjacent rooms or corridors. 1.6 cfm/square foot or 4 air changes minimum for laboratories. Design temperature for offices and laboratory areas of 72°F will be maintained year round with humidity at 30% (IS) in winter and 50% (IS) in summer. The HVAC system will be constructed of "institutional" grade materials. (First-class materials)

Horizontal supply distribution ducts will be sized and provided with capped tees at 10'-6" intervals to accommodate future supply box additions to facilitate changes.

Air system will be designed to accommodate one chemical fume hood per laboratory module with an additional future capacity of 50% (i.e., one additional hood for each two hoods initially installed).

Heating medium will be via MCO underground high pressure steam lines and pumped condensate return mains from the NOATP power plant via an extension of the existing utility tunnel.

Steam distributed at medium or low pressure will produce hot water for zone reheat boxes and domestic hot water via heat exchanges. Clean steam for autoclaves will be produced by steam-to-steam generator or by electric steam generators at each autoclave room.

Chilled water will be produced in the CEM building by open-drive type chillers and cooling towers, pumps and appurtenances. Chilled water will be generated with a 12 degree temperature differential (42-54°F). Provision will be made to tie the CEM chillers into a future campus chilled water loop system.

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CENTER FOR ENVIRONMENTAL MEDICINE  
PROGRAM DOCUMENT

Process condenser water will be available to be supplied to cold room condensers, laboratory equipment and water cooled compressors.

A heat recovery system will reclaim heat from exhaust air via liquid medium piped transfer to air intake location.

Fume hood exhaust will be a "ganged" system. The general laboratory and support space exhaust air shall be combined with the general fume hood exhaust in the penthouse. Individual fume hood exhaust ducts will rise separately up to the penthouse, where the accessible exhaust valve will be located. Air will be discharged through exhaust air fans through stacks which shall be at least 16'-0" higher than the penthouse roof. Space will be provided at penthouse level at each individual hood duct for future HEPA and charcoal filters. Fume hood exhaust flow rate shall be 100 fpm across sash opening at full height. Five fume hoods will be separately ducted and exhausted and have special uses.

Each darkroom with an autodeveloper to have developer vent. Glasswash room to have special exhaust canopy over equipment.

The building will have an approved smoke evacuation system.

The building (or individual suites) will be capable of occupied/unoccupied HVAC modes.

The Animal Facility will be separately exhausted with special exhaust filters, 15 air changes per hour and constant volume. Design temperature of 65°F will be maintained winter and summer at 35%-65% humidity-adjustable. Each cage room will have three ceiling exhaust ports for connection to microisolator animal cage system racks.

This building will tie into the central management system already in place at CMO.

#### ELECTRICAL

Power will be supplied via the existing electrical substation adjacent to parking lot #4. Transformers and primary switchgear will be located in the basement level of CEM building. A minimum of 50% space capacity will be designed into the incoming secondary service and service equipment to accommodate future expansion. The building will have two feeders into a double-ended substation.

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CENTER FOR ENVIRONMENTAL MEDICINE  
PROGRAM DOCUMENT

Laboratory power distribution should be made by means of bus duct runs from transformer substation secondaries with plug-in circuit breakers for convenient distribution to individual labs.

The distribution design will have the capability of converting an office space into a laboratory. Each laboratory module shall be served by a panelboard with a shunt-trip main breaker for emergency shut-down where required. Panel board bussing, number of breakers and feeders shall be sized based on design loads, plus 50% capacity for growth. In no case will panel board bus and feeder size be sized less than 100 amperes. The project will provide a ground bus for each panel board.

Normal Power-Design Criteria:

Lighting, Receptacles and Laboratory Equipment	15 watts/sf
HVAC & Plumbing	6 watts/sf
Chiller Plant	<u>9 watts/sf</u>
Total Connected	30 watts/sf

A diversity factor should not be planned as all equipment may be on at the same time.

Electrical distribution on walls and work benches will be by surface-mounted large capacity wireways that accept standard devices and outlets. Each lab and office shall be provided with an isolated ground bus system and a computer-grade central ground system.

Emergency Power - Provide one diesel oil-fired emergency generator set with automatic transfer switching to provide emergency power for:

- Egress lighting
- Selected laboratory receptacles
- Selected cold rooms
- Elevators
- Fumehood fans
- Animal facility ventilation
- Fire pump and other fire code requirements
- Security system



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PROGRAM DOCUMENT

Telephone and Data - Central data and communications rooms stacked serving each floor to accommodate fiber-optic trunk, ethernet, etc., with additional spare empty conduits and horizontal distribution via fully accessible, ceiling cable tray. Density will be approximately two combined voice and data outlets for every 120 ASF.

Lighting will be supplied at 277 volts. Lighting will generally be fluorescent, 3500° K color temperature and electronic energy-saving ballasts. Light levels shall be in accordance with IES Standards.

The building will have a complete lightning protection system.

Security and Special Alarms

A card-key access system shall be provided for use by laboratory personnel to gain entry to the building at certain hours. Access to the Animal Facility and other designated interior doors will also be by card-key.

An alarm system is required for hazardous material holding areas.

Illuminated warning signs are required for doors into x-ray, laser and other potentially hazardous work areas.

Fire alarm control panel tie-in required to nearest campus interface point.

PLUMBING

Water distribution to originate from lines in Arlington Avenue. System to have code complaint backflow prevention. System to have separate domestic and laboratory water supply systems for cold water, hot water and hot water recirculation.

Hot water supplied by independent steam-fired semi-instantaneous type water heaters to deliver 140° F water. Hot water may alternately be supplied by gas-fired hot water heaters.

Drainage system for laboratory waste to be separate from domestic plumbing fixtures. Lab waste to be acid neutralized before connecting to sanitary sewer systems as per city code.

Storm drainage to be independent from sanitary system and receive discharge from all roof drains and other devices receiving direct rain or storm water. System will discharge into the site storm drainage system.

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CENTER FOR ENVIRONMENTAL MEDICINE  
PROGRAM DOCUMENT

Central piped lab compressed air system, non-medical type, generated with triplex, oil-less, rotary compressors, providing 0 to 360 SCFM at 100 psig.

Central piped lab vacuum system consisting of duplex rotary vane vacuum pumps providing 0 to 160 ACFM at 15 inches mercury.

Emergency Fixtures Emergency eyewash units to be provided at one location per laboratory, deck-mounted paddle-type.

Emergency showers to be provided in each laboratory and in each corridor at not more than 100 foot intervals, solid rod and ring operation.

All normal and emergency plumbing fixtures to meet ADA requirements.

Central Reverse Osmosis (RO)/Deionized (DI) Water System will be piped to one sink in each lab and will provide one megohm lab grade water.

Natural gas piped system to selected locations in each laboratory. System to originate from gas mains in Tech. Park roadways.

All Chemical fume hoods to have cold water, cup sink, compressed air, natural gas and lab vacuum.

#### FIRE PROTECTION

Automatic wet sprinkler fire protection system for entire building complying with NFPA and local fire department recommendations for light hazard occupancy.

Sprinkler system flow switches to annunciate water flow for two zones per floor.

Standpipes will be provided in stairs to comply with codes.

Hydrants located adjacent to fire truck access routes on two sides of the building.

Siamese connections adjacent to fire truck access on two sides of the building.

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CENTER FOR ENVIRONMENTAL MEDICINE  
PROGRAM DOCUMENT

Fire pump to be located at ground level of the building, rated for 1,000 GPM at 65 psig boost pressure, electric motor driven, to comply with codes.

**STRUCTURAL DESIGN**

The structural frame of the CEM Building can be either poured-in-place reinforced concrete or steel construction. A very stiff frame is necessary to provide acceptable vibration limits for sensitive equipment. Areas may, in addition, be zoned on a floor for potential very strict vibration limits for electron microscopes or laser labs.

Corridors should be separated from vibration sensitive lab areas by a column line to avoid foot-fall vibration.

Since the CEM Building will probably begin as a freestanding structure, the floor-to-floor heights can be established on the basis of required mechanical space and room heights; 15'-0" is a likely minimum floor-to-floor height to allow economical horizontal duct and piping distribution. Clear room heights should be a minimum of 9'-0" everywhere and not less than half the width of larger rooms.

Live loading should be a minimum of 100 psf in general with 150 psf for core areas including equipment rooms.

The column bay will generally be about 21' x 21' to 24',

Shear walls should be allowed only in permanently obscured locations: behind elevators, along stairway walls and exterior walls along the sides of lab modules. Exterior walls will be in high demand for windows.

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CENTER FOR ENVIRONMENTAL MEDICINE  
PROGRAM DOCUMENT

9. ARCHITECTURAL SYSTEMS OUTLINE

PARTITIONS:

- Interior partitions at ground floor (basement level) support areas to be CMU sealed and painted: Epoxy paint in animal facility areas and chemical and biological holding areas.
- Interior partitions at 1st through X floor levels to be metal stud with 5/8" gypsum wall board.
- Rated walls to be multiple layers of rated gypsum wallboard (shaftwall assembly) construction.
- All studs extend up to structure above.
- All office, restroom and conference room walls to have acoustical insulation.

CEILINGS:

- Ceilings in entrance lobby areas, classrooms, restrooms, animal facility and chemical and biological holding areas to be gypsum wall board construction or accessible lay-in ceilings.
- All other areas to have suspended lay-in 2' x 2' acoustical tile ceilings, except cold rooms which have special ceiling plenum construction provided with cold room.

FLOORING:

- Flooring in lobby area to be smooth surface stone pavers.
- Flooring in restrooms to be ceramic mosaic tile.
- Flooring in autoclave rooms, glasswash room and animal facility rooms to be seamless resinous flooring (Dex-O-Tex).
- Flooring in corridors, laboratories, tissue culture rooms instrument rooms, break rooms, housekeeping closets and darkrooms to be vinyl composition tile. (VCT)
- Classroom, offices, conference rooms to be carpeted.
- Cold rooms have rubber mat flooring.

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CENTER FOR ENVIRONMENTAL MEDICINE  
PROGRAM DOCUMENT

- Flooring in electrical closets, tel/data closets, receiving and storage areas to be hardened concrete.

CASEWORK:

- Lab casework will be a modular component system either custom wood or steel C-frame system.
- All casework and laboratory cabinetwork to be AWI premium grade wood construction with select white maple veneer, solid maple edgebanding.
- Lab benchtops to be 3/4" thick white epoxy resin.
- Desktops and shelving to have chemical-resistant plastic laminate surfacing.
- Autoclave, glasswash, cold room, animal procedure and necropsy counters to be stainless steel with integral stainless steel sinks.
- Lab bench and instrument room shelving to be stainless steel wire shelving in modular widths and depths on heavy-duty wall standards.

WOODWORK:

- Interior doors with lites to be solid maple rail and stile construction.
- Interior doors without lites to be maple veneer, solid core wood construction.
- Offices to have wall-mounted wood veneer shelving, areas of tackboard and marker boards typical.

HARDWARE:

- Hardware to be heavy-duty institutional type with lever handles, brushed stainless steel finish, keyed to MCO master system.

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PROGRAM DOCUMENT

- All hardware in animal facility to be stainless steel/corrosion proof construction. All outside corners on corridor walls to have stainless steel corner guards, and all doors to have stainless steel armor plate. All animal facility doors to be hollow metal, 8'-0" clear height openings.

ELEVATORS:

- Three elevators to be provided, two passenger and one to be sized for service capacity, connecting all floors. Service elevator extends to mechanical penthouse level.
- Service elevator cab size to be 5' x 9' with (hospital size to accommodate gurney) 4,500 lb. capacity.
- Interior cab and door/frame to be satin-finished stainless steel.

EXTERIOR CLADDING/SOFFITS:

- Exterior cladding to be masonry/precast concrete panel construction.
- Exterior soffits to be insulated exterior cementitious finish system.

WINDOWS:

- Windows to be modular sized aluminum frame units with 15% operable sash panels, all insulated glazing.
- Frame finish to be Kynar coating in one color.

VENTILATION:

- Air intake louvers and fume hood system exhaust stacks to be shop coated Kynar finish.

ROOFING:

- Rubber membrane sheet roofing over rigid roof insulation.

SITEWORK:

- Existing site contours and any large existing trees are to be preserved as much as possible

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PROGRAM DOCUMENT

- Provide on site storm drainage system.
- Provide trees, shrubs, planting and grass areas with an irrigation system.
- Screen loading dock and apron area around it with 5' high masonry walls compatible with the building cladding materials.
- Fire water hydrants and siamese connections as required by the local fire department.
- Poured concrete pedestrian walkways leading to entrances and parking areas. (Complying with ADA)
- Hard-surface employee and guest parking for 170 cars.

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PROGRAM DOCUMENT

10. CONSTRUCTION COST BUDGET

Construction cost is a major driver of the size of the CEM building. The budget identified below is the result if the space needs identified in part 5, the engineering description in part 8, the architectural description in part 9, and the general site requirements set forth in NOATP Development Criteria. The budget is adjusted for a Spring 1995 bid date.

Gross building area: 53,000

Construction Cost per Gross Square Foot: \$220-230

Construction Cost Budget: \$11,660,000 - \$12,190,000

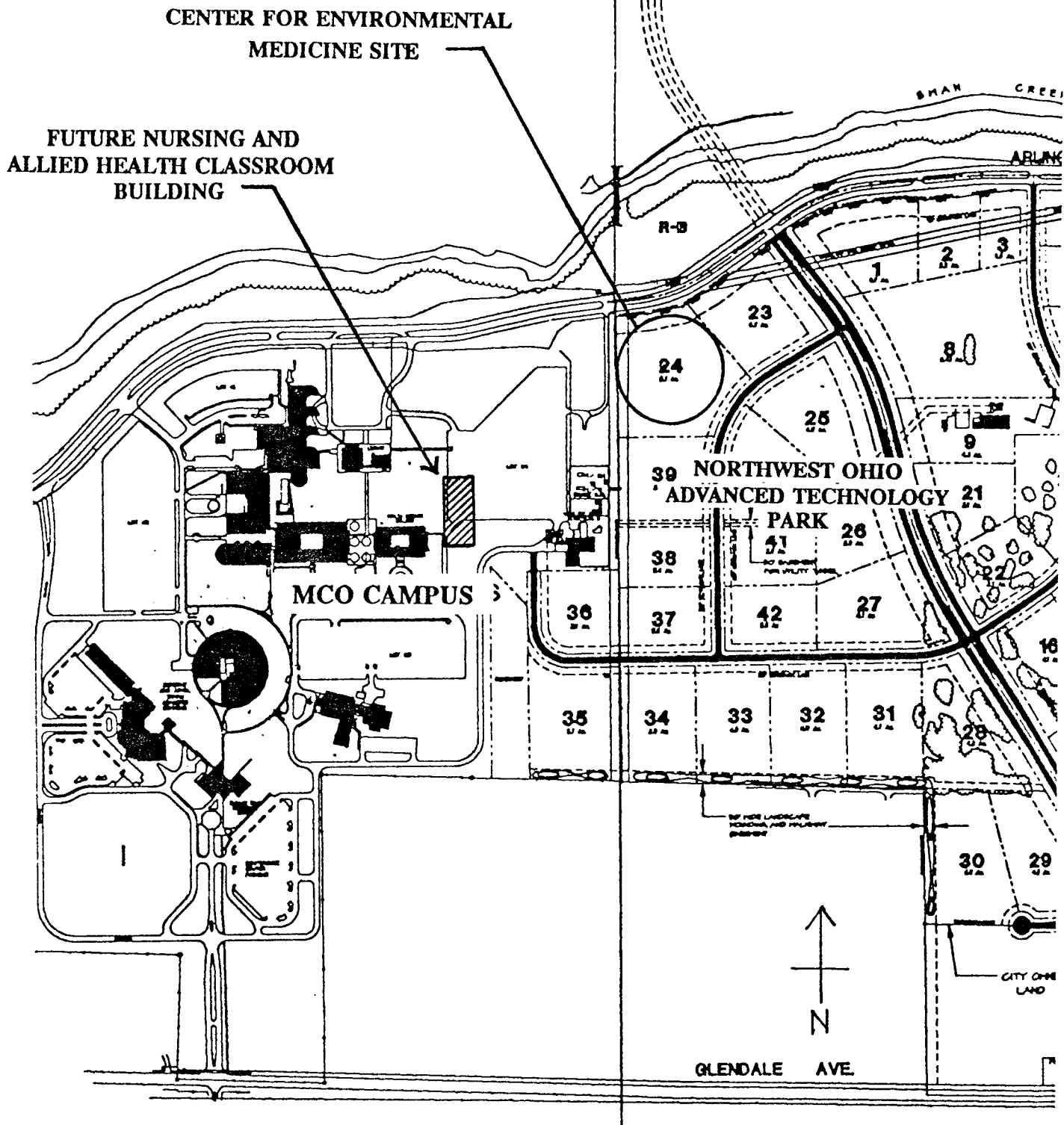
This budget includes:

1. Group I fixed equipment such as autoclaves, fumehoods, laboratory casework, built-in darkroom equipment, projection screens, and animal facility cagewasher.

This budget does not include:

1. Moveable furnishings such as desks, tables, chairs, copiers, refrigerators, or microwave ovens.
2. Window blinds or shades.
3. Interior and exterior signage.
4. Audio-visual equipment in lecture and conference rooms.
5. Telephone instruments





SITE PLAN

MEDICAL COLLEGE OF OHIO  
 CENTER FOR ENVIRONMENTAL MEDICINE  
 PROGRAM DOCUMENT

11. PRELIMINARY SPACE SUMMARY WITH  
 PRINCIPAL INVESTIGATORS REQUESTS

SKETCH NO.	PERSONS	ROOM	NSF	QTY	EXTENSION
<b>DR. PEREIRA</b>					
2	1 P.D. 3 Grad. 2 Tech.	Molecular Biology Lab (1½ Modules)	850	1	850
2	1 P.D. 1 Grad. 2 Tech.	Biochemistry Lab (1 Module)	567	1	567
10	1 Tech.	High Hazard Suite (½ Module)			
		Paying Room	142	1	142
		Additive Mixing Room	142	1	142
9	1 Tech.	Bacteria Culture Room (¼ Module) 1 Laminar Flow Hood 2 Incubators	142	1	142
9	1 Tech.	Mammalian T.C. Room (¼ Module) (Human)	142	1	142
9	1 Tech.	Mammalian T.C. Room (¼ Module) (Animal)	142	1	142
	---	Animal Room - Rats - 1 See Animal Facility			
	---	Animal Room - Mice -1 See Animal Facility			
4	1 P.I.	Office	165	1	165

MEDICAL COLLEGE OF OHIO  
CENTER FOR ENVIRONMENTAL MEDICINE  
PROGRAM DOCUMENT

SKETCH NO.	PERSONS	ROOM	NSF	QTY	EXTENSION
6	3 P.D.	Post. Doc. Group Office	165	1	165
6	4 Grad.	Group Office	165	1	165
6	4 Tech.	Group Office	165	1	165
6	2 SR.P.	Offices	165	2	330
	---	-40° Freezer Room	115	1	115
Total 28 Persons			Subtotal 3,232 NSF		
DR. OLSON					
2	1-2 Tech. 1-2 Grad.	Biochemistry Labs (2 modules) minus 70° C Freezers 2-Refrigerators 1-5' Chemical Hood Cell Culture - 2-4' Lam. Hood 1-Incubator	1,134	2	22,268
2	2 Techs. 2 Grad.	Empirical Fluid Mechanics (1½ Modules) Engineering Lab (Lasers, High-Tech Inst.)	850	1	850
26	2 Tech.	Computational Lab (¼ Module) High-Tech Computers Files	142	1	142
4	4 P.I.	Offices	165	4	660
25	---	Pulmonary Function Lab Exercise Bike, Treadmill	210	1	210
	---	Waiting Area	80	1	80
5	1 Tech.	Office	116	1	116

**CENTER for ENVIRONMENTAL MEDICINE  
MEDICAL COLLEGE OF OHIO  
OCTOBER 6, 1994  
PRELIMINARY SPACE SUMMARY**

SKETCH NO.	PERSONS	ROOM	NSF	QTY	EXTENSION
6	---	Group Office 4 Grad. desks	165	1	165
	---	Aquatic Room - 2 Modular Cage Rooms (See Animal Facility)			
2	2-3 Techs 2-3 Grads	Soils Labs (½ Modules) Exposure Lab Controlled Environments (Modular Cage Room in Animal Facility)	851	1	851
	---	Immunosuppressed Animal Room (See Animal Facility)			
Total 21 Persons				Subtotal	5,342 NSF
<b>DR. MING YOU</b>					
3	8-10 Per.	Molecular Carcinogenesis Lab (2 Modules) 1 Tissue Culture Hood 2 5' Chemical Fume Hood	1,134	1	1,134
4	1 P.I.	Office	165	1	165
8	---	Staff Office 10 Computer Terminals	378	1	378
	---	Modular Cage Rooms - 3 (See Animal Facility)			
Total 11 Persons				Subtotal	1,677 NSF
<b>DR. FORNEY</b>					
3	24 Per.	Toxicology Lab (4 Modules) 4 - 5' Chemical Fume Hoods 1 Canopy Hood	2,268	1	2,268

**CENTER for ENVIRONMENTAL MEDICINE  
MEDICAL COLLEGE OF OHIO  
OCTOBER 6, 1994  
PRELIMINARY SPACE SUMMARY**

SKETCH NO.	PERSONS	ROOM	NSF	QTY	EXTENSION
11	---	Record Storage Room	200	1	200
12	---	Specimen Storage Room Refrigerators	200	1	200
4	1 P.I.	Office	165	1	165
5	2 PhD.	Offices	116	2	232
5	1 Super	Supervisor's Office	116	1	116
6	4 P.D.	Post. Doc. Shared Office 4 Desks Files	165	1	165
Total 32 Persons			Subtotal 3,346 NSF		
DR. SCHUT					
2	8-10 Per.	Molecular Biology Lab (3 Modules) 1 - 5' Chemical Hood 1 - 6' Laminar Flow Hood	1,701	1	1,701
4	1 P.I.	Office	165	1	165
6	4 P.D.	Group Office	165	1	165
Total 15 Persons			Subtotal 2,031 NSF		
DR. RUCH					
2	8 Per.	Molecular Biology Lab (2 Modules)	1,134	1	1,134
9	1 Per.	Tissue Culture Room (¼ Module) 1 6' Laminar Flow Hood	142	1	142

**CENTER for ENVIRONMENTAL MEDICINE  
 MEDICAL COLLEGE OF OHIO  
 OCTOBER 6, 1994  
 PRELIMINARY SPACE SUMMARY**

SKETCH NO.	PERSONS	ROOM	NSF	QTY	EXTENSION
	1 Per.	Microbiology Lab (1/2 Module) 1-6' Laminar Flow Hood	284	1	284
16	---	Fluorescence Microscope	45	1	45
4	1 P.I.	Office	165	1	165
6	4 P.D.	Post. Doc. Shared Office 4 Desks Files	165	1	165
		Modular Cage Room - 1 @ 150 (See Animal Facility)			
	Total 15 Persons				Subtotal 1,935 NSF
	<b>DR. GUNNING</b>				
3	4-6 Per.	Molecular Biology Lab (1 Module)	567	1	567
4	1 P.I.	Office	165	1	165
	Total 7 Persons				Subtotal 732 NSF
	<b>SHARED ON EACH FLOOR (ASSUME 2 LAB FLOORS)</b>				
13	---	Conference/Library Room	240	2	480
7	3 Per.	Support Office	250	2	500
14	---	Process Darkroom	130	2	260
15	---	Copier Nook	24	2	48
17	---	Cold Room	115	2	230
18	---	Equipment Room (1/2 module)	284	2	568

**CENTER for ENVIRONMENTAL MEDICINE  
MEDICAL COLLEGE OF OHIO  
OCTOBER 6, 1994  
PRELIMINARY SPACE SUMMARY**

SKETCH NO.	PERSONS	ROOM	NSF	QTY	EXTENSION
19	---	Autoclave Room 2 Medium Autoclaves	160	2	320
17	---	Cold/Warm Rooms	115	2	230
20	---	Break Room with Kitchenette	200	2	400

Each Floor will Have:

- Appropriate Toilet Rooms
- Housekeeping Closet
- Electrical Room
- Data & Phone Room
- Tank Closet?
- Some Storage

Total 1 Person	Subtotal	3,036 NSF
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**CORE FACILITIES**

**1. INHALATION FACILITY (ADJACENT TO ANIMAL FACILITY)**

---	Cage Rooms (Mice or Rats)	200	2	400
1 Tech.	Control Room (2-2'x4' Chambers)	120	1	120
---	Animal Surgical Suite			
---	O.R.	115	1	115
---	Prep/Recovery Room	115	1	115
---	Instrument Storage	60	1	60

Total 1 Person	Subtotal	810 NSF
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**2. ELECTRON MICROSCOPY SUITE**

21	---	E.M. Rooms 2 TEM Rooms 1 HR, FEG, BEI, EDS Room	180	3	540
----	-----	---	-----	---	-----

**CENTER for ENVIRONMENTAL MEDICINE  
MEDICAL COLLEGE OF OHIO  
OCTOBER 6, 1994  
PRELIMINARY SPACE SUMMARY**

SKETCH NO.	PERSONS	ROOM	NSF	QTY	EXTENSION
	---	Confocal Microscope Room (1/4 Module)	142	1	142
	1 Tech.	Office	80	1	80
	---	Prep. Room (6' Chemical Hood)	115	1	115
	---	Storage	60	1	60
	---	Fine Section Room (4 Stations) Sink, Work Counter	230	1	230
	---	Conference Room	115	1	115
	---	Dark Rooms Counter, Sink	50	3	150
	---	Power Room	50	1	50
	---	Copy Stand Room	115	1	115
				Subtotal	1,597 NSF
		<b>3. CENTRAL DNA LAB</b>			
2	1 Per	DNA Synthesis Lab (1 Module) Synthesizer 1 - 5' Chemical Hood Tech. Desk Area	567	1	567
	Total 1 Person			Subtotal	567 NSF
		<b>BUILDING SUPPORT</b>			
22	---	Large Conference Room 12 Seats	382	1	382
23	---	Lecture Room 30 Seats	600	1	600



**CENTER for ENVIRONMENTAL MEDICINE  
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SKETCH NO.	PERSONS	ROOM	NSF	QTY	EXTENSION
5	1 Per.	Receiving Office (2 Bay Loading Dock)	116	1	116
	---	Vending Area & Break Room	180	1	180
	---	Waste Chemical Holding 4' Fume Hood	142	1	142
	---	Isotope Holding	80	1	80
	---	Chemical Storage Receiving and Dispensing	200	1	200
	---	Tank Holding	80	1	80
	---	Mail Room	120	1	120
24	1 Per.	Central Classwashing 1 Large Autoclave 2 Medium Autoclaves 1 Glasswasher 1 Glassdryer Double sink Sorting Table	370	1	370
24	1 Per.	Small Office	80	1	80
	---	Storage for Glasswashing	80	1	80
	2 Per.	Building Management Office	200	1	200
	---	General Storage	800	1	800
	---	Graphic Arts Facility Next to Dark Room on one floor	200	1	200
Total 5 Persons			Subtotal 3,630 NSF		

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SKETCH

NO.	PERSONS	ROOM	NSF	QTY	EXTENSION
-----	---------	------	-----	-----	-----------

27	---	Modular Cage Rooms 4 Racks each = 800 Mice 300 Rats or Olson -2 Rms 96 Rabbits Pereira-2 Rms X Fish Ming You-3 Rms Tanks Ruch-1 Rm Gunning-4 Rms Schut - 1 Rm	150	14	2,100
----	-----	---	-----	----	-------

4	1 Per.	Office	165	1	165
---	--------	--------	-----	---	-----

28	---	Restrooms, Shower, Lockers (Men and Women)	135	2	270
----	-----	---	-----	---	-----

29	2 Per.	Cage Washing Room Cage Washer (6' x 9') Rinsing Area Rack Holding Bottle Filling J. Hopper Hooded Dump Station	575	1	575
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---	Food and Bedding Storage	80	1	80
-----	--------------------------	----	---	----

---	Trash Holding Room	80	1	80
-----	--------------------	----	---	----

---	Rack and Cage Storage	200	1	200
-----	-----------------------	-----	---	-----

---	Procedure Room 1 Laminar Flow Hood	165	1	165
-----	---------------------------------------	-----	---	-----

---	Immunosuppressed Animal Room Suites (BL-3 potential)	230	2	460
-----	--	-----	---	-----

27		1 - Cage Room @ 150 1 - Anteroom @ 80 Sink			
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Total 3 Persons

Subtotal 4,095 NSF

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TOTAL 142 PEOPLE

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132 Researchers  
18 Lab Modules  
241 NSF/Researcher  
397 GSF/Researcher

TOTAL  
FACTOR N TO G

32,030 NSF  
1.65  
52,850 GSF

Average researchers  
per P.I.:19  
Average 2.6 modules  
per P.I.

At 7 principal investigators:  
Average 3,036 NSF (Not including  
Animal facilities or core facilities)  
15 P.I.s = 58,150 ASF or 95,952 GSF  
15 P.I.s @ 2.6 modeules each = 39 Modules

AIR FORCE OF SCIENTIFIC RESEARCH (AFSC)

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Jan Boggs  
STINFO Program Manager

Approved for public release;  
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